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LOGINID:ssspta1187mxw

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 3	MAR 16	CASREACT coverage extended
NEWS 4	MAR 20	MARPAT now updated daily
NEWS 5	MAR 22	LWPI reloaded
NEWS 6	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 7	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 8	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 9	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 10	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 12	MAY 01	New CAS web site launched
NEWS 13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20	JUN 29	STN Viewer now available
NEWS 21	JUN 29	STN Express, Version 8.2, now available
NEWS 22	JUL 02	LEMBASE coverage updated
NEWS 23	JUL 02	LMEDLINE coverage updated
NEWS 24	JUL 02	SCISEARCH enhanced with complete author names
NEWS 25	JUL 02	CHEMCATS accession numbers revised
NEWS 26	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 27	JUL 16	CAplus enhanced with French and German abstracts

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:14:57 ON 16 JUL 2007

=> file medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 12:15:09 ON 16 JUL 2007

 FILE LAST UPDATED: 14 Jul 2007 (20070714/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s angiosarcoma or hemangioendothelioma or (basal (w) cell(w)carcinoma) or
(squamous (w)cell(w)carcinoma or (malignant(w)melanoma)
UNMATCHED LEFT PARENTHESIS 'OR (SQUAMOUS'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s angiosarcoma or hemangioendothelioma or (basal (w) cell(w)carcinoma) or
(squamous (w)cell(w)carcinoma) or (malignant(w)melanoma)
          2941 ANGIOSARCOMA
          2766 HEMANGIOENDOTHELIOMA
        186460 BASAL
       2149614 CELL
        423069 CARCINOMA
          4843 BASAL (W) CELL(W)CARCINOMA
         97447 SQUAMOUS
       2149614 CELL
        423069 CARCINOMA
         31393 SQUAMOUS (W)CELL(W)CARCINOMA
        205328 MALIGNANT
         65040 MELANOMA
         16344 MALIGNANT(W)MELANOMA
L1       56469 ANGIOSARCOMA OR HEMANGIOENDOTHELIOMA OR (BASAL (W) CELL(W)CARCIN
               OMA) OR (SQUAMOUS (W)CELL(W)CARCINOMA) OR (MALIGNANT(W)MELANOMA)

=> s angiogenesis
L2       30688 ANGIOGENESIS

=> s l1 and l2
L3         702 L1 AND L2

=> s Kaposi? or psoriasis or lymphangiogenesis or hemangioma or (Sturge(w) Weber)
or (verruca(w) vulgaris) or neurofibromatosis or (tuberous(w)sclerosis) or
(pyrogenic(w)granuloma?)
         11285 KAPOSI?
         23695 PSORIASIS
           646 LYMPHANGIOGENESIS
         21262 HEMANGIOMA
          1107 STURGE
          4948 WEBER
          1096 STURGE(W) WEBER
           763 VERRUCA
         21873 VULGARIS
           238 VERRUCA(W) VULGARIS
          9783 NEUROFIBROMATOSIS
          5058 TUBEROUS
         70885 SCLEROSIS
          4613 TUBEROUS(W)SCLEROSIS
          1823 PYROGENIC
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          51344 GRANULOMA?
              2 PYROGENIC(W)GRANULOMA?
L4        71291 KAPOSI? OR PSORIASIS OR LYMPHANGIOGENESIS OR HEMANGIOMA OR (STUR
                GE(W) WEBER) OR (VERRUCA(W) VULGARIS) OR NEUROFIBROMATOSIS OR
               (TUBEROUS(W)SCLEROSIS) OR (PYROGENIC(W)GRANULOMA?)

=> s l4 and l2
L5          926 L4 AND L2

=> s (recessive(w)dystrophic (w)epidermolysis(w)bullosa) or (venous(w)ulcers) or
acne or rosacea or exzema or (molluscum(w)contagious) or (seborrheic(w)keratosis)
or (actinic(w)keratosis)
          35142 RECESSIVE
           7661 DYSTROPHIC
           3679 EPIDERMOLYSIS
           3827 BULLOSA
            299 RECESSIVE(W)DYSTROPHIC (W)EPIDERMOLYSIS(W)BULLOSA
         130821 VENOUS
          32937 ULCERS
            745 VENOUS(W)ULCERS
           9705 ACNE
           1737 ROSACEA
             13 EXZEMA
           1299 MOLLUSCUM
           3154 CONTAGIOUS
              1 MOLLUSCUM(W)CONTAGIOUS
           2969 SEBORRHEIC
           8273 KERATOSIS
            379 SEBORRHEIC(W)KERATOSIS
           2632 ACTINIC
           8273 KERATOSIS
            598 ACTINIC(W)KERATOSIS
L6        12978 (RECESSIVE(W)DYSTROPHIC (W)EPIDERMOLYSIS(W)BULLOSA) OR (VENOUS(W
                )ULCERS) OR ACNE OR ROSACEA OR EXZEMA OR (MOLLUSCUM(W)CONTAGIOUS
               ) OR (SEBORRHEIC(W)KERATOSIS) OR (ACTINIC(W)KERATOSIS)

=> s l6 and l2
L7             32 L6 AND L2

=> d ab 1-10

L7   ANSWER 1 OF 32      MEDLINE on STN
AB   Cetuximab is a chimeric immunoglobulin G1 monoclonal antibody that targets
     the extracellular domain of the epidermal growth factor receptor (EGFR)
     with high specificity and affinity. It competitively inhibits endogenous
     ligand binding and thereby inhibits subsequent EGFR activation. The EGFR
     signaling pathways regulate cell differentiation, proliferation,
     migration, angiogenesis and apoptosis, all of which become
     deregulated in cancer cells. EGFR is an important target for cancer
     therapy and many studies have demonstrated that cetuximab is active in
     several types of cancer, particularly colorectal and head and neck cancer.
     Cetuximab enhances the effects of many standard cytotoxic agents,
     including irinotecan, and in combination with chemotherapy it can elicit
     antitumor responses in tumors that previously failed to respond to that
     chemotherapy. Cetuximab also enhances radiation-induced apoptosis. On
     the basis of a pivotal European randomized study (the BOND study) and of 2
     clinical studies conducted in the USA, cetuximab has been approved in
     combination with irinotecan for patients affected by EGFR-expressing
     metastatic colon cancer after failure with irinotecan. There have only
     been a few small phase II trials on first-line treatment in metastatic
     colorectal cancer, but the results suggest promising activity of cetuximab
     together with irinotecan or oxaliplatin. There is some evidence that
     additive efficacy can be achieved using EGFR inhibitors in combination
     with vascular endothelial growth factor receptor inhibitors such as
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bevacizumab. A correlation between response and the main toxicity (acne-like skin reaction) has been observed but is unclear. EGFR status as a specific marker for EGFR inhibitors is controversial. At the moment, EGFR expression does not appear to be a predictive factor for response to EGFR inhibitors.

L7 ANSWER 2 OF 32 MEDLINE on STN

AB Vitamins A and D are the first group of substances that have been reported to exhibit properties of skin hormones, such as organized metabolism, activation, inactivation, and elimination in specialized cells of the tissue, exertion of biological activity, and release in the circulation. Vitamin A and its two important metabolites, retinaldehyde and retinoic acids, are fat-soluble unsaturated isoprenoids necessary for growth, differentiation and maintenance of epithelial tissues, and also for reproduction. In a reversible process, vitamin A is oxidized IN VIVO to give retinaldehyde, which is important for vision. The dramatic effects of vitamin A analogues on embryogenesis have been studied by animal experiments; the clinical malformation pattern in humans is known. Retinoic acids are major oxidative metabolites of vitamin A and can substitute for it in vitamin A-deficient animals in growth promotion and epithelial differentiation. Natural vitamin A metabolites are vitamins, because vitamin A is not synthesized in the body and must be derived from carotenoids in the diet. On the other hand, retinoids are also hormones - with intracrine activity - because retinol is transformed in the cells into molecules that bind to and activate specific nuclear receptors, exhibit their function, and are subsequently inactivated. The mechanisms of action of natural vitamin A metabolites on human skin are based on the time- and dose-dependent influence of morphogenesis, epithelial cell proliferation and differentiation, epithelial and mesenchymal synthetic performance, immune modulation, stimulation of angiogenesis and inhibition of carcinogenesis. As drugs, vitamin A and its natural metabolites have been approved for the topical and systemic treatment of mild to moderate and severe, recalcitrant acne, photoaging and biologic skin aging, acute promyelocytic leukaemia and Kaposi's sarcoma. On the other hand, the critical importance of the skin for the human body's vitamin D endocrine system is documented by the fact that the skin is both the site of vitamin D (3)- and 1,25-dihydroxyvitamin D (3) [1, 25(OH) (2)D (3)]-synthesis and a target organ for 1,25(OH) (2)D (3). 1,25(OH) (2)D (3) is not only essential for mineral homeostasis and bone integrity, but also for numerous further physiologic functions including regulation of growth and differentiation in a broad variety of normal and malignant tissues, including cells derived from prostate, breast and bone. In keratinocytes and other cell types, 1,25(OH) (2)D (3) regulates growth and differentiation. Consequently, vitamin D analogues have been introduced for the treatment of the hyperproliferative skin disease psoriasis. Other newly detected functions of vitamin D analogues include profound effects on the immune system as well as protection against cancer and other diseases, including autoimmune and infectious diseases, in various tissues. Current investigation of the biological effects of vitamin D analogues are likely to lead to new therapeutic applications that, besides cancer prevention, may include the prevention and treatment of infectious as well as of inflammatory skin diseases. This review summarizes existing knowledge on vitamins A and D, the major vitamin-hormones of the skin.

L7 ANSWER 3 OF 32 MEDLINE on STN

AB ABSTRACT: BACKGROUND: This study was conducted to evaluate the immunohistochemical (IHC) expression of interleukin 8 (IL-8) in skin biopsies of inflammatory acne vulgaris (IAV) in an attempt to understand the disease pathogenesis. MATERIALS AND METHODS: A total of 58 biopsies, 29 from lesional IAV and 29 normal non lesional sites were immunostained for IL-8. The intensity of staining was evaluated in the epidermis and dermis and was scored as mild, moderate and severe. The expression was correlated with the clinical grade, disease course and

histological changes. RESULTS: IL-8 immunoreactivity was expressed in lesional IAV compared to non lesional skin biopsies ($p < 0.001$). Increased expression was significantly associated with epidermal hyperplasia and follicular hyperkeratosis ($p < 0.001$). In addition, the more pronounced IL-8 expression of the dermal endothelial cells and neutophilic inflammatory infiltrate correlated with dermal angiogenesis and the extent of dermal inflammatory response ($p < 0.001$). Moreover, increased dermal immunoreactivity paralleled progressive course ($p = 0.02$) but not the duration of the disease. CONCLUSION: We were able to demonstrate altered immunoreactivity of IL-8 in IAV compared to normal skin. Targeted therapy to block IL-8 production may hold promise in limiting the deleterious effects of IL-8-mediated inflammatory response and angiogenesis.

L7 ANSWER 4 OF 32 MEDLINE on STN

AB The Ras-Raf-MEK-ERK signalling pathway is frequently dysregulated in human malignancies, as is angiogenesis and the vascular endothelial growth factor receptor (VEGF/VEGFR) pathway. These kinases are therefore important anticancer targets. The novel, oral treatment sorafenib (BAY 43-9006), has been shown to be an inhibitor of VEGFR, Raf and platelet-derived growth factor in clinical trials against a variety of cancers, with the greatest activity to date observed in metastatic renal cancer. Although side-effects with this targeted therapy are usually not dose-limiting, they frequently involve the skin, and consist of a maculopapular rash, palmar-plantar dysaesthesia, alopecia and xerosis. In this report, we present two patients in whom treatment with sorafenib resulted in inflammation of actinic keratosis, which in some cases progressed to invasive squamous cell carcinoma. This side-effect is of clinical importance, as early recognition is critical for early treatment and may represent a source of additional morbidity to these patients.

L7 ANSWER 5 OF 32 MEDLINE on STN

AB OBJECTIVE: Many factors impair healing of chronic venous ulcer (CVU), and many theories have been proposed to explain their pathogenesis. Coagulation factor XIII (FXIII) influences tissue regeneration and angiogenesis with effects on wound healing. Because FXIII properties depend upon its genetic variants, we investigated whether intragene polymorphisms may have modulating effects on the CVU area. METHODS: The study included 121 patients with nonhealing CVUs (CEAP clinical class C6) that included 67% with primary chronic venous disease (CVD), 26% with post-thrombotic ulcers, and 7% with mixed ulcer origin. Polymerase chain reaction was used to genotype them for Val34Leu, Pro564Leu, and Tyr204Phe variants in the FXIII-A subunit gene and for His95Arg variant in the FXIII-B subunit gene. The same variants were analyzed in 102 controls, healthy subjects who were case-matched by age and gender. RESULTS: Genotype distribution for all polymorphisms investigated was not significantly different between cases and controls. Conversely, our CVU cases had a mean ulcer area inversely related with the presence of both Leu34 and Leu564 alleles (ValVal, 12.3 +/- 22.4 cm2 vs LeuLeu, 3.9 +/- 2.6 cm2, P = .002; ProPro, 10.2 +/- 21.2 cm2 vs LeuLeu, 2.9 +/- 1.4 cm2, P = .002). In combined analysis, those cases who were wild-type for both variants (ValVal34/ProPro564) had a further increase in mean ulcer size compared with cases carrying both variants (Leu34/Leu564) (13.3 +/- 27.1 cm2 vs 5.2 +/- 5.6 cm2; P = .034). CONCLUSIONS: No correlation exists between FXIII genotypes and the prevalence of chronic venous ulcers, thus demonstrating that FXIII polymorphisms have no role in ulcer development. In contrast, FXIII-gene variants, in particular the non-wild-type alleles Leu34 and Leu564, were associated with a smaller venous ulcer surface and might have favorable effects on reparative processes.

L7 ANSWER 6 OF 32 MEDLINE on STN

AB Venous ulcers are a major health problem because of

the increased costs of the treatment and the refractory nature of the ulcers. The treatment cost is estimated to be around 1 billion dollars per year in the United States (US), and the average cost for one patient over a lifetime exceeds dollars 400,000. There has been an increasing trend in the use of growth factors in their management. Genetic engineering has revolutionised the research of wound healing, as the majority of recombinant growth factors are now available for in vitro and in vivo studies. Online searches of Medline, Pub Medical and Embase were carried out using the terms venous ulcers, leg ulcers, growth factors and growth hormone. The literature regarding the potential role of growth factors in the management of leg ulcers is reviewed. The important clinical studies are critically analysed with a view to appreciate the emerging therapies and the further research possibilities in the management of venous leg ulcers. Clinical results with the use of growth factors in non-healing wounds are encouraging. However, small sample sizes and inconsistent end points in different clinical studies have been the main hurdle in reaching a definite conclusion. Further research is needed to provide the definite evidence. Future developments may include different delivery methods for the growth factors, use of different combinations of growth factors administered simultaneously or, sequentially, bioengineered skin grafts and chemical induction of angiogenesis with the use of gene transfer techniques.

L7 ANSWER 7 OF 32 MEDLINE on STN

AB Wound healing is a complex process resulting from an interplay of processes including coagulation, inflammation, angiogenesis, and epithelialization. The chemokine family has been shown to contain members that are potent regulators of many of these pathways. Because we have previously shown that chemokines "pool" in biologic wound dressings, we studied the levels of CXC and CC chemokines, along with key inflammatory mediators, serially from a group of patients undergoing therapy for chronic venous leg ulcers. After 8 weeks, all patients had marked clinical healing of their ulcers (median 63.3% reduction in size) with two of 10 completely healed. Wound fluids extracted from dressings showed high levels of platelet factor-4 and interferon-gamma-inducible protein, with a trend toward increases in the ratio of the sums of the angiogenic versus angiostatic CXC chemokines ($p = 0.082$) in the tissues collected from the center of the ulcers during wound closure. Neutrophil-activating peptide-2 and interleukin-8 accounted for the most changes in wound fluid angiogenic chemokines, with significant differences both as compared with baseline levels and with patients' plasma level noted at various time points between weeks 0 and 8. The level of angiostatic chemokines, interferon-y inducible protein 10 and platelet-activating-4, fell most significantly between weeks 0 and 3 as compared with plasma levels. The observed shift toward angiogenic CXC chemokines suggests that effective healing in chronic venous insufficiency ulcers appears to "move" the ulcer bed toward a state more conducive to epithelialization,characteristic of the proliferative phase of wound healing. CC chemokines were also elevated at baseline in the wound fluid samples as compared with the patients' plasma levels. Macrophage inflammatory protein-1 (3 and regulated on activation, normal T expressed and secreted (RANTES) levels decreased with healing, whereas there were significant increases in the tissue levels of monocyte chemoattractant protein-1 and macrophage inflammatory protein-1 a over the first 4 weeks of therapy ($p<$ or $= 0.05$ for both). Coincident with these changes was a steady increase in the ratio of interleukin-1 R/interleukin-1 receptor antagonist protein in the ulcer center tissues, which also correlated with healing ($p < 0 .05$) as compared with a decreasing ratio at the ulcer edge, and a biphasic response in the wound fluids. These findings suggest that advanced wound care techniques help move the ulcer from a chronic inflammatory state into one more characteristic of the late inflammatory/early proliferative phase of wound healing. Chemokines may play a critical role in the pathogenesis of chronic venous ulcers through their effects on angiogenesis and/or the progression of inflammatory reactions at

the site of injury.

L7 ANSWER 8 OF 32 MEDLINE on STN

AB C225 (cetuximab) is a monoclonal antibody that targets the epidermal growth factor receptor (EGF-R). It is used for the treatment of solid malignant tumors in advanced stages. It works against tumors by inhibiting cell proliferation, angiogenesis and the formation of metastases, as well as by promoting cell apoptosis. We present the case of a 64-year-old male patient affected with a colon neoplasm with hepatic metastases, for which treatment with cetuximab was indicated. He came to our department because of a skin eruption with papules and pustules located on the face, neck, presternal area and upper back, but with no cysts or comedones. The biopsy was compatible with an acneiform eruption. The patient was treated with minocycline, 100 mg/day for 2 weeks, with the clinical symptoms responding favorably. When he was given further doses of cetuximab, he once again presented with new eruptions, but of lesser intensity. Because of the high frequency with which this adverse effect appears, it is recommended that cetuximab be included on the list of drugs causing acneiform eruptions.

L7 ANSWER 9 OF 32 MEDLINE on STN

AB Tetracyclines are broad-spectrum antibiotics that act as such at the ribosomal level where they interfere with protein synthesis. They were first widely prescribed by dermatologists in the early 1950s when it was discovered that they were effective as a treatment for acne. More recently, biologic actions affecting inflammation, proteolysis, angiogenesis, apoptosis, metal chelation, ionophoresis, and bone metabolism have been researched. The therapeutic effects of tetracycline and its analogues in various diseases have also been investigated. These include rosacea, bullous dermatoses, neutrophilic diseases, pyoderma gangrenosum, sarcoidosis, aortic aneurysms, cancer metastasis, periodontitis, and autoimmune disorders such as rheumatoid arthritis and scleroderma. We review the nonantibiotic properties of tetracycline and its analogues and their potential for clinical application.

L7 ANSWER 10 OF 32 MEDLINE on STN

AB Summary Background Granulocyte/macrophage colony-stimulating factor (GM-CSF), a cytokine with pleiotropic functions, has been successfully employed in the treatment of chronic skin ulcers. The biological effects underlying GM-CSF action in impaired wound healing have been only partly clarified. Objectives To investigate the effects of GM-CSF treatment of chronic venous ulcers on lesion vascularization and on the local synthesis of the angiogenic factors vascular endothelial growth factor (VEGF) and placenta growth factor (PlGF). Methods Patients with nonhealing venous leg ulcers were treated with intradermal injection of recombinant human GM-CSF, and biopsies were taken at the ulcer margin before and 5 days after administration. Wound vascularization was analysed by immunohistochemistry using antiplatelet endothelial cell adhesion molecule-1/CD31 and anti-alpha-smooth muscle actin antibodies. VEGF and PlGF transcription was assessed by in situ hybridization. To identify the cell populations transcribing VEGF within the ulcer bed, the VEGF hybridization signal was correlated with the immunostaining for different cell type markers on serial sections. Direct induction of VEGF transcription by GM-CSF was investigated in GM-CSF-treated cultured macrophages and keratinocytes. Results Blood vessel density was significantly increased in the ulcer bed following GM-CSF treatment. VEGF transcripts were localized in keratinocytes at the ulcer margin both before and after GM-CSF treatment, whereas a VEGF hybridization signal was evident within the ulcer bed only following administration. PlGF mRNA was barely detectable in keratinocytes at the ulcer margin and was not visibly increased after treatment. Unlike VEGF, a specific PlGF hybridization signal could not be detected in cells within the ulcer following GM-CSF administration. Monocytes/macrophages were the main cell population transcribing VEGF after GM-CSF treatment. In vitro analysis demonstrated

that VEGF transcription can be directly stimulated by GM-CSF in a differentiated monocytic cell line, but not in keratinocytes. Conclusions Our data show that increased vascularization is associated with GM-CSF treatment of chronic venous ulcers and indicate that inflammatory cell-derived VEGF may act as an angiogenic mediator of the healing effect of GM-CSF in chronic ulcers.

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=> s curcumin
L8          1951 CURCUMIN

=> d his

     (FILE 'HOME' ENTERED AT 12:14:57 ON 16 JUL 2007)

     FILE 'MEDLINE' ENTERED AT 12:15:09 ON 16 JUL 2007
L1         56469 S ANGIOSARCOMA OR HEMANGIOENDOTHELIOMA OR (BASAL (W) CELL(W)CAR
L2         30688 S ANGIOGENESIS
L3           702 S L1 AND L2
L4         71291 S KAPOSI? OR PSORIASIS OR LYMPHANGIOGENESIS OR HEMANGIOMA OR (S
L5           926 S L4 AND L2
L6         12978 S (RECESSIVE(W)DYSTROPHIC (W)EPIDERMOLYSIS(W)BULLOSA) OR (VENOU
L7            32 S L6 AND L2
L8          1951 S CURCUMIN

=> s l8 and (l3 or l5 or l7)
L9             5 L8 AND (L3 OR L5 OR L7)

=> d 1-5

L9   ANSWER 1 OF 5     MEDLINE on STN
AN   2007357544      MEDLINE
DN   PubMed ID: 17569219
TI   Beneficial role of curcumin in skin diseases.
AU   Thangapazham Rajesh L; Sharma Anuj; Maheshwari Radha K
CS   Uniformed Services University of Health Sciences, Bethesda, MD, USA..
     rlthangapazham@usuhs.mil
NC   G174KT
SO   Advances in experimental medicine and biology, (2007) Vol. 595, pp.
     343-57.  Ref: 78
     Journal code: 0121103. ISSN: 0065-2598.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
     (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
     (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
     General Review; (REVIEW)
LA   English
FS   Priority Journals
EM   200707
ED   Entered STN: 19 Jun 2007
     Last Updated on STN: 4 Jul 2007
     Entered Medline: 3 Jul 2007

L9   ANSWER 2 OF 5     MEDLINE on STN
AN   2005433072      MEDLINE
DN   PubMed ID: 16098028
TI   Naturally occurring proteasome inhibitors from mate tea (Ilex
     paraguayensis) serve as models for topical proteasome inhibitors.
AU   Arbiser Jack L; Li Xing-Cong; Hossain Chowdhury Fiaz; Nagle Dale G; Smith
     David M; Miller Paul; Govindarajan Baskaran; DiCarlo Josh; Landis-Piwowar
     Kristin R; Dou Q Ping
CS   Department of Dermatology, Emory University School of Medicine, Atlanta,
     Georgia 30322, USA.. jarbise@emory.edu
NC   P30 AR 42687 (NIAMS)
```

R01 47901
R03AR44947 (NIAMS)
SO The Journal of investigative dermatology, (2005 Aug) Vol. 125, No. 2, pp. 207-12.
Journal code: 0426720. ISSN: 0022-202X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 16 Aug 2005
Last Updated on STN: 14 Sep 2005
Entered Medline: 13 Sep 2005

L9 ANSWER 3 OF 5 MEDLINE on STN
AN 2004348663 MEDLINE
DN PubMed ID: 15252836
TI Inhibition of growth and survival of human head and neck squamous cell carcinoma cells by curcumin via modulation of nuclear factor-kappaB signaling.
AU Aggarwal Sita; Takada Yasunari; Singh Sujay; Myers Jeffrey N; Aggarwal Bharat B
CS Cytokine Research Laboratory, Department of Bioimmunotheraphy, The University of Texas M. D. Anderson Cancer Center, Houston, Texas, USA.. aggarwal@mdanderson.org
NC 1P50-CA97007-02 (NCI)
P01 CA91844 (NCI)
SO International journal of cancer. Journal international du cancer, (2004 Sep 20) Vol. 111, No. 5, pp. 679-92.
Journal code: 0042124. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200408
ED Entered STN: 15 Jul 2004
Last Updated on STN: 1 Sep 2004
Entered Medline: 31 Aug 2004

L9 ANSWER 4 OF 5 MEDLINE on STN
AN 2003062768 MEDLINE
DN PubMed ID: 12572355
TI Chemopreventive effect of tea and curcumin on DMBA-induced oral carcinogenesis in hamsters.
AU Li Ning; Chen Xiaoxin; Han Chi; Chen Junshi
CS Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine, Beijing 100050, China.
NC CA56673 (NCI)
SO Wei sheng yan jiu = Journal of hygiene research, (2002 Oct) Vol. 31, No. 5, pp. 354-7.
Journal code: 9426367. ISSN: 1000-8020.
CY China
DT (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA Chinese
FS Priority Journals
EM 200308

ED Entered STN: 8 Feb 2003
Last Updated on STN: 20 Aug 2003
Entered Medline: 19 Aug 2003

L9 ANSWER 5 OF 5 MEDLINE on STN
AN 2002435184 MEDLINE
DN PubMed ID: 12151348
TI Inhibition of 7,12-dimethylbenz[a]anthracene (DMBA)-induced oral carcinogenesis in hamsters by tea and curcumin.
AU Li Ning; Chen Xiaoxin; Liao Jie; Yang Guangyu; Wang Su; Josephson Youssef; Han Chi; Chen Junshi; Huang Mou-Tuan; Yang Chung S
CS Laboratory for Cancer Research, College of Pharmacy, Rutgers, The State University of New Jersey, 164 Frelinghuysen Road, Piscataway, NJ 08854, USA.
NC CA 56673 (NCI)
SO Carcinogenesis, (2002 Aug) Vol. 23, No. 8, pp. 1307-13.
Journal code: 8008055. ISSN: 0143-3334.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200209
ED Entered STN: 24 Aug 2002
Last Updated on STN: 6 Sep 2002
Entered Medline: 5 Sep 2002

=> s collagenase(w)inhibito?)
UNMATCHED RIGHT PARENTHESIS 'INHIBITO?)'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s (collagenase(w)inhibito?)
16402 COLLAGENASE
881127 INHIBITO?
L10 281 (COLLAGENASE(W)INHIBITO?)

=> s l10 and (l3 or l5 or l7)
L11 1 L10 AND (L3 OR L5 OR L7)

=> d

L11 ANSWER 1 OF 1 MEDLINE on STN
AN 95101158 MEDLINE
DN PubMed ID: 7528513
TI Angiogenic potential in vivo by Kaposi's sarcoma cell-free supernatants and HIV-1 tat product: inhibition of KS-like lesions by tissue inhibitor of metalloproteinase-2.
AU Albini A; Fontanini G; Masiello L; Tacchetti C; Bigini D; Luzzi P; Noonan D M; Stetler-Stevenson W G
CS National Institute of Research on Cancer, Genoa, Italy.
SO AIDS (London, England), (1994 Sep) Vol. 8, No. 9, pp. 1237-44.
Journal code: 8710219. ISSN: 0269-9370.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals; AIDS
EM 199501
ED Entered STN: 15 Feb 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 30 Jan 1995

=> d ab\
'AB\' IS NOT A VALID FORMAT FOR FILE 'MEDLINE'

The following are valid formats:

The default display format is BIB.

ABS ---- AB
ALL ---- AN, DN, TI, AU, CS, NC, SO, CM, CY, DT, LA, FS, NCT, OS,
EM, ED, AB, ST, CT, NA, RN, CN, GEN
BIB ---- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
CBIB --- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, NCT, OS, EM, ED
DALL --- ALL, delimited for post processing
IABS --- ABS, with a text label
IALL --- ALL, indented with text labels
IBIB --- BIB, indented with text labels
IND ---- ST, CT, NA, RN, CN, GEN
TRIAL -- TI, ST, CT, NA, RN, CN, GEN
(SAM, TRI, FREE)
HIT ---- All fields containing hit terms
HITIND - IND
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms

Hit terms will be highlighted in all available fields except CM and PY.

To display a particular field or fields, enter the display field codes. For a list of display field codes, enter 'HELP DFIELDS' at an arrow prompt (=>). Examples of formats include: 'BIB'; 'AB'; 'SO,ST'. You may specify the format fields in any order, and the information will be displayed in the same order as the format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be used with the DISPLAY ACC command to display the record for a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):ab

L11 ANSWER 1 OF 1 MEDLINE on STN
AB OBJECTIVE: To determine the neoplastic nature of Kaposi's sarcoma (KS). A highly vascularized lesion, KS is frequently associated with AIDS, indicating HIV products may be involved. DESIGN AND METHODS: We determined the angiogenic properties of KS cell-secreted products and the HIV-1-tat gene product in vivo. Cell-free secreted products (KS-CM) from cultured epidemic and sporadic KS spindle cells or recombinant (r) HIV-1 tat protein were injected into mice with a matrix support (Matrigel). RESULTS: KS-CM produced lesions carrying all the phenotypic hallmarks of KS, as observed by light and electron microscopy: spindle-shaped cells, haemorrhages and an inflammatory infiltrate, as well as Factor VIII-positive endothelial cells lining new blood vessels. Electron microscopy indicated an initial granulocyte invasion, with spindle-cell migration and neocapillary formation in the centre of the matrix. These lesions required the cofactor heparin; KS-CM or heparin alone were poorly angiogenic. A less intense angiogenesis, with lower cellularity and few granulocytes, was observed in basic fibroblast growth factor (bFGF)/heparin lesions, indicating that factors other than bFGF are present in the KS spindle-cell products. When the collagenase inhibitor tissue inhibitor of metalloproteinases (TIMP)-2 was added to the sponges, KS-CM-induced angiogenesis was reduced by approximately 65% and bFGF-induced angiogenesis inhibited completely. Recombinant HIV-1 tat protein, a growth factor for KS cells, induced vascularization that was also

enhanced by heparin, implying that HIV-1 tat could contribute to the aetiology of HIV-associated KS. CONCLUSIONS: KS-like lesions were obtained by injecting cell-free secreted products, suggesting that KS is a 'self-propagating' proliferative lesion caused by a cytokine imbalance and not a true neoplasm. Heparin-binding factors appear to be involved, and HIV-1 tat angiogenic properties implicate this molecule in AIDS-associated KS. Inhibition of KS-CM-induced KS-like lesions by TIMP-2 suggests that metalloproteinase inhibitors could be potential therapeutic agents for KS.

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=> s fumagillin or sulfated or aminophenylphosphonic or oxindole
          317 FUMAGILLIN
         7350 SULFATED
            7 AMINOPHENYLPHOSPHONIC
          258 OXINDOLE
L12       7932 FUMAGILLIN OR SULFATED OR AMINOPHENYLPHOSPHONIC OR OXINDOLE

=> s l12 and (l3 or l5 or l7)
L13         16 L12 AND (L3 OR L5 OR L7)

=> d 16

L13  ANSWER 16 OF 16     MEDLINE on STN
AN   90100565     MEDLINE
DN   PubMed ID: 1688470
TI   Inhibition of angiogenesis by recombinant human platelet
     factor-4 and related peptides.
AU   Maione T E; Gray G S; Petro J; Hunt A J; Donner A L; Bauer S I; Carson H
     F; Sharpe R J
CS   Repligen Corporation, Cambridge, MA 02139.
SO   Science (New York, N.Y.), (1990 Jan 5) Vol. 247, No. 4938, pp. 77-9.
     Journal code: 0404511. ISSN: 0036-8075.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199002
ED   Entered STN: 28 Mar 1990
     Last Updated on STN: 29 Jan 1996
     Entered Medline: 5 Feb 1990

=> d ab 16

L13  ANSWER 16 OF 16     MEDLINE on STN
AB   Recombinant human platelet factor-4 (rhPF4), purified from Escherichia
     coli, inhibited blood vessel proliferation in the chicken chorioallantoic
     membrane in a dose-dependent manner. Treatment of several cell types with
     rhPF4 in vitro suggested that the angiostatic effect was due to specific
     inhibition of growth factor-stimulated endothelial cell proliferation.
     The inhibitory activities were associated with the carboxyl-terminal,
     heparin-binding region of the molecule and could be abrogated by including
     heparin in the test samples, an indication that sulfated
     polysaccharides might modulate the angiostatic activity of platelet
     factor-4 in vivo. Understanding of the mechanisms of control of
     angiogenesis by endogenous proteins should facilitate the
     development of effective treatments for diseases of pathogenic
     neovascularization such as Kaposi's sarcoma, diabetic
     retinopathy, and malignant tumor growth.

=> d ab 1-15

L13  ANSWER 1 OF 16     MEDLINE on STN
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AB Lipoic acid (LA) is a sulfated antioxidant produced physiologically as a coenzyme of the pyruvate dehydrogenase complex; it is currently used for treatment of non-insulin-dependent diabetes to favor the cellular uptake of glucose. We have previously described the angiopreventive potential of molecules sharing common features with LA: N-acetyl cysteine, epigallocatechin-3-gallate and xanthohumol. To expand these studies, we have tested the capacity of LA to modulate angiogenesis in tumor growth using a Kaposi's sarcoma model. Endothelial cells exposed to LA displayed a dose-dependent reduction of cell migration and a time-dependent modulation of the phosphorylation of key signaling molecules. In vivo, LA efficiently repressed angiogenesis in matrigel plugs and KS-Imm tumor growth. We analyzed modulation of gene expression in endothelial cells treated with LA for 5 h (early response), finding a mild anti-apoptotic, antioxidant and anti-inflammatory response. A group of LA-targeted genes was selected to perform real-time polymerase chain reaction time-lapse experiments. The long-term gene regulation (48 h and 4 days) shows higher rates of modulation as compared with the array data, confirming that LA is able to switch the regulation of several genes linked to cell survival, inflammation and oxidative stress. LA induced the production of tumor necrosis factor-alpha-related apoptosis-inducing ligand (TRAIL) in KS-Imm and activin-A in KS-Imm and endothelial cells; these factors show anti-angiogenic activity in vivo contributing to explain the inhibitory effect of LA on neovascularization. According to our data, LA has promising anti-angiogenic properties, though its influence on central metabolic pathways should suggest more caution about its widespread and not prescribed use at pharmacological doses.

L13 ANSWER 2 OF 16 MEDLINE on STN

AB Resveratrol, trans-3,5,4'-trihydroxystilbene, was first isolated in 1940 as a constituent of the roots of white hellebore (Veratrum grandiflorum O. Loes), but has since been found in various plants, including grapes, berries and peanuts. Besides cardioprotective effects, resveratrol exhibits anticancer properties, as suggested by its ability to suppress proliferation of a wide variety of tumor cells, including lymphoid and myeloid cancers; multiple myeloma; cancers of the breast, prostate, stomach, colon, pancreas, and thyroid; melanoma; head and neck squamous cell carcinoma; ovarian carcinoma; and cervical carcinoma. The growth-inhibitory effects of resveratrol are mediated through cell-cycle arrest; upregulation of p21Cip1/WAF1, p53 and Bax; down-regulation of survivin, cyclin D1, cyclin E, Bcl-2, Bcl-xL and cIAPs; and activation of caspases. Resveratrol has been shown to suppress the activation of several transcription factors, including NF-kappaB, AP-1 and Egr-1; to inhibit protein kinases including IkappaBalpha kinase, JNK, MAPK, Akt, PKC, PKD and casein kinase II; and to down-regulate products of genes such as COX-2, 5-LOX, VEGF, IL-1, IL-6, IL-8, AR and PSA. These activities account for the suppression of angiogenesis by this stilbene. Resveratrol also has been shown to potentiate the apoptotic effects of cytokines (e.g., TRAIL), chemotherapeutic agents and gamma-radiation. Phamacokinetic studies revealed that the target organs of resveratrol are liver and kidney, where it is concentrated after absorption and is mainly converted to a sulfated form and a glucuronide conjugate. In vivo, resveratrol blocks the multistep process of carcinogenesis at various stages: it blocks carcinogen activation by inhibiting aryl hydrocarbon-induced CYP1A1 expression and activity, and suppresses tumor initiation, promotion and progression. Besides chemopreventive effects, resveratrol appears to exhibit therapeutic effects against cancer. Limited data in humans have revealed that resveratrol is pharmacologically quite safe. Currently, structural analogues of resveratrol with improved bioavailability are being pursued as potential therapeutic agents for cancer.

L13 ANSWER 3 OF 16 MEDLINE on STN

AB The interaction of glycosaminoglycans (GAG) with peptides relies on

noncovalent binding to basic amino acid sequences, for which a minimal requirement is a pentapeptide region in the protein and the sulfated and carboxyl region in the GAG. Since such sequences are present in the heparin-binding angiogenic cytokines, including hepatocyte growth factor (HGF), we have postulated that such small peptides may have biological activity. Two basic peptide regions of the beta chain of HGF (RYRNKH512-516, HHRGK645-649) exhibited significant antiangiogenic activity in vivo in the chorioallantoic membrane assay and showed some antiproliferative activity in vitro on normal human brain microvessel endothelial-but not on anchorage-independent endothelial-cells (Kaposi sarcoma). Basic HIV-TAT peptides and scrambled hexapeptides did not show similar activity, except for KRKRKR, indicating sequence specificity of the phenomena. An HGF-derived basic peptide, HHRGK, modulated tumor-induced angiogenesis in vivo by interfering with the morphogenic, but not with the proliferative, phase of the process. These observations suggest small basic peptides as a new class of angiogenesis modulators.

L13 ANSWER 4 OF 16 MEDLINE on STN
AB TNP-470, an analogue of fumagillin, has been shown to inhibit angiogenesis in vitro and in vivo. In 1992, TNP-470 entered clinical development for cancer as an anti-angiogenic agent. It is currently in Phase I/II trials in Kaposi's sarcoma, renal cell carcinoma, brain cancer, breast cancer, cervical cancer and prostate cancer. In early clinical reports, TNP-470 is tolerated up to 177 mg/m(2) with neurotoxic effects (fatigue, vertigo, ataxia, and loss of concentration) being the principal dose limiting toxicity (DLT). Terminal half-life values are short and have shown intermittent and intrapatient variation (range: 0.05 - 1.07 h). Recently, mechanistic studies have identified cell cycle mediators and the protein methionine aminopeptidase-2 (MetAP-2) as molecular targets of TNP-470 and fumagillin. Animal studies confirm some toxic effects on normal angiogenic processes such as the female reproductive system and wound healing, which will require caution and close monitoring in the clinic. TNP-470 is one of the first anti-angiogenic compounds to enter clinical trials, making it a valuable prototype for future trials of angiogenesis inhibitors in oncology.

L13 ANSWER 5 OF 16 MEDLINE on STN
AB The antitumor effect of the angiogenesis inhibitor TNP470, O-(chloro-acetyl-carbamoyl) fumagillol, a synthetic analogue of fumagillin, was studied in vitro and in vivo on, cell line KB which produced interleukin (IL)-8. In vitro, TNP470 reduced the production of IL-8 from KB cells, the same as anti-IL-8 antibody (Ab.) The combination of anti-IL-8 Ab (10 micrograms/ml) and TNP470 (10 ng/ml) significantly inhibited the proliferation of KB cells, compared to no treatment ($p < 0.05$). Proliferation of KB cells was also significantly more suppressed by simultaneous treatment of cisplatin and TNP470 (1 mg/ml), than cisplatin alone. The in vivo antitumor effect of TNP470 was studied using anti-IL-8 Ab, anti-vascular endothel growth factor (VEGF) Ab, and TNP470, in administered by different routes, i.e., intratumoral (i.t.), intraperitoneal (i.p.), and intravenous. TNP470 (10 mg/ml) showed an antitumor effect, and intratumoral administration of TNP470 was the most effective route. Combined administration of anti-IL-8 Ab (i.p.) and TNP470 (i.t.) reduced tumor volume more than anti-IL-8 Ab alone did. These results suggest that the combination of TNP470, cisplatin, and anti-IL-8 Ab could be a beneficial treatment for solid tumors of the head and neck.

L13 ANSWER 6 OF 16 MEDLINE on STN
AB Delivery of the sulfated polysaccharide dextrin 2-sulfate by the intraperitoneal route to the lymphatic circulation resulted in a clinically significant improvement in Kaposi's sarcoma in three

patients. Our in vitro studies show that although sulfated dextrins do not interfere with the growth of isolated human umbilical vein endothelial cells, they do inhibit the morphological differentiation of endothelial cells into tubes as well as reduce new vessel formation in a placental angiogenesis assay. The antiangiogenic effect of dextrin 6-sulfate is greater than that of dextrin 2-sulfate and is independent of their anti-human immunodeficiency virus type 1 activities.

L13 ANSWER 7 OF 16 MEDLINE on STN

AB Tumor angiogenesis is a fundamental step in tumor growth and proliferation. Fumagillin is an anti-angiogenic agent which is secreted by Aspergillus, but is also toxic. A fumagillin analogue, TNP-470, has been developed which is a potent angiogenic inhibitor with few side effects. TNP-470 has inhibited tumor growth in Lewis lung cancer and melanoma in animal models. This study was designed to test this proven anti-angiogenic agent's effects on head and neck cancer growth. Fort,v Harlan nude mice were injected subcutaneously with cancer cells from a human oral squamous cell carcinoma. After 3 weeks of tumor growth 25 mice were injected with TNP-470 subcutaneously at a distant site every other day for 30 days while 10 control mice received saline injections. Five mice began TNP-470 injections at the time of tumor injection to determine if TNP-470 can prevent tumor development. The tumor growth and development was unaffected by TNP-470 as compared to the control group. Therefore, the use of an angiogenic inhibitor had no effect on oral cancer growth. Analysis of the cell line utilized found abnormal mRNA expression, which included high p53 expression and low cyclin D1 expression. These results suggest that oral cancers are less dependent on angiogenesis than other tumor types. The genetic abnormalities may explain the angiogenesis independence that was demonstrated. Results found in other tumor types with angiogenic inhibitors cannot be extrapolated to oral cancer since genetic mutations may allow oral tumors to grow without neovascularization.

L13 ANSWER 8 OF 16 MEDLINE on STN

AB PURPOSE: Angiogenesis is a major component of Kaposi's sarcoma (KS) and a critical process in tumor growth. The present study was designed primarily to test the toxicity and pharmacokinetics (PK) of the angiogenesis inhibitor TNP-470 and secondarily to evaluate tumor response in patients with early AIDS-related KS. PATIENTS AND METHODS: Patients with AIDS-related KS were required to have cutaneous disease with > or = 5 measurable lesions and no evidence of pulmonary, symptomatic gastrointestinal, or acutely life-threatening KS. Thirty-eight patients received TNP-470 by weekly intravenous infusion over 1 hour at one of six dose levels for up to 24 weeks. RESULTS: The dose levels tested included 10, 20, 30, 40, 50 and 70 mg/m2. Median CD4 count was 24 cells/microl (range, 0 to 460). Fourteen patients (36%) had > or = 50 cutaneous lesions and 19 (49%) had oral lesions. Adverse events included neutropenia (n = 2), hemorrhage (n = 3), and urticaria (n = 1). PK studies showed wide interpatient and intrapatient variability. Elimination half-life values were short (range, 0.01 to 0.61 hours). Seven patients (18%) achieved a partial response. The median time to partial response was 4 weeks (range, 2 to 25), and the median duration of response was 11 weeks (range, 3 to 26+). CONCLUSION: TNP-470, administered as a weekly, 1-hour infusion to patients with early AIDS-KS is well-tolerated at doses up to and including the highest dose tested. Tumor responses were observed in a substantial number of cases and occurred at various dose levels. TNP-470 should be evaluated further in patients with AIDS-KS as a single agent and in combination with other biologic response modifiers in early disease or after initial response to cytotoxic chemotherapy.

L13 ANSWER 9 OF 16 MEDLINE on STN

AB STUDY OBJECTIVE: To characterize the pharmacokinetic profile of TNP-470, a

synthetic analog of fumagillin that is a potent inhibitor of angiogenesis and inhibits neovascularization in several solid tumor models. DESIGN: A dose-escalation phase I clinical trial. SETTING: The National Institutes of Health. PATIENTS: Patients with human immunodeficiency virus-associated Kaposi's sarcoma. INTERVENTIONS: The TNP-470 dosage was increased in 13 sequential cohorts using a modified Fibonacci escalation scheme (4.6, 9.3, 15.4, 23.2, and 43.1 mg/m2). The drug was administered as a 1-hour intravenous infusion. Serial blood samples were collected and assayed by reverse-phase high-performance liquid chromatography and the pharmacokinetics were characterized. MEASUREMENTS AND MAIN RESULTS: There was a linear relationship between the dose of TNP-470 and both area under the curve to infinity (AUC[inf]) and time to maximum concentration (Cmax). The Cmax ranged between 6.6 ng/ml at the lowest dosage (4.6 mg/m2) and 597.1 ng/ml at the highest dosage (43.1 mg/m2). The agent was rapidly cleared from the circulation with a short terminal half-life (0.88 +/- 2.5 hr), which is consistent with preclinical data. Peak plasma concentrations of AGM-1883, an active metabolite, ranged between 0.4 and 158.1 ng/ml. CONCLUSION: Concentrations of TNP-470 that have in vitro activity were achievable in vivo. The drug was rapidly cleared from the circulation after a single 1-hour infusion. There was considerable interpatient variability in the clearance, but no evidence of saturable elimination. If more prolonged exposure is necessary for activity, administration of TNP-470 by continuous infusion may be suitable.

L13 ANSWER 10 OF 16 MEDLINE on STN

AB BACKGROUND: Tecogalan sodium is an angiogenesis inhibitor isolated from a sulfated polysaccharide produced by the bacterium Arthrobacter. The antiangiogenic effect of tecogalan sodium is thought to be mediated by the inhibition of binding of basic fibroblast growth factor to cellular receptors. PATIENTS AND METHODS: A phase I study was conducted in thirty-three patients with refractory malignancies, including AIDS-associated Kaposi's sarcoma. Patients received a single i.v. infusion every three weeks with the infusion duration ranging from one to twenty-four hours. Seven different dosage levels were studied (125, 185, 240, 300, 390, 445, and 500 mg/m2). RESULTS: The primary dose-limiting toxicity was prolongation of the activated partial thromboplastin time with peak times being between 1.0-4.0 times the upper limit of normal. This toxicity was ameliorated at a given dose level by prolonging the infusion time. Other common toxicities included fever (40%) and rigors (31%) which were well controlled with acetominophen and meperidine. The serum half-life of tecogalan sodium was between 1-1.5 hours and < 25% of unchanged drug was excreted in the urine. CONCLUSIONS: The recommended phase II dose of tecogalan sodium on this schedule is 390 mg/m2 over 24 hours. Other schedules including continuous administration should be investigated to maximize the efficacy of this novel angiogenesis inhibitor.

L13 ANSWER 11 OF 16 MEDLINE on STN

AB The antiangiogenic effect of tecogalan sodium on corneal neovascularization was investigated. Tecogalan sodium, a sulfated polysaccharide peptidoglycan complex isolated from an Arthrobacter species, has been reported to inhibit angiogenesis induced by basic fibroblast growth factor (bFGF) as well as tumor angiogenesis related to Kaposi's sarcoma. Corneal neovascularization induced by bFGF was inhibited by tecogalan sodium in a dose-dependent manner. Since bFGF is known to have a promoting effect on corneal neovascularization, tecogalan sodium may be possible therapeutic agent for corneal neovascularization, which can cause severe visual disturbances.

L13 ANSWER 12 OF 16 MEDLINE on STN

AB Hemangioma and other angiomatous diseases of childhood are common. Although most lesions are harmless and self-limiting, some are

associated with significant morbidity and may be life-threatening. Interferon-alpha, a weak angiogenesis inhibitor, recently has been found to significantly reduce the mortality rate associated with life-threatening hemangiomas. The effectiveness of AGM-1470, a potent inhibitor of angiogenesis derived from the fungal product fumagillin, was tested in a mouse model of hemangioendothelioma. Thirty syngeneic mice were implanted with cells derived from a spontaneous mouse hemangioendothelioma. Tumors formed within 2 to 3 days, and the animals were then treated systemically with AGM-1470 or with saline and vehicle alone. After 22 days, the tumor volume in the saline-treated mice was 7368 +/- 2723 mm3, versus 709 +/- 73 mm3 in the mice that received AGM-1470 (P < .001). Survival was prolonged for the AGM-1470-treated mice, and there was no evidence of drug-related toxicity. All experiments were repeated. In this study, AGM-1470 was safe and highly effective in the treatment of hemangioendothelioma. AGM-1470, and other antiangiogenic agents, may provide safe and effective treatment for hemangioma and other angiomatous diseases.

L13 ANSWER 13 OF 16 MEDLINE on STN
AB OBJECTIVE: To determine whether the anti-angiogenesis agent DS-4152 inhibits the replication of HIV-1 in vitro. DESIGN: A sulfated polysaccharide-peptidoglycan DS-4152 has recently been identified as a potent and selective inhibitor of Kaposi's sarcoma (KS). Therefore, it is important to evaluate the anti-HIV-1 activity of DS-4152 alone and in combination with dideoxynucleosides. METHODS: Activity of DS-4152 against HIV-1 replication was examined in MT-4, Molt-4, and peripheral blood lymphocyte cells. The inhibitory effect of the compound on syncytium-formation was determined by cocultivation of Molt-4 cells with Molt-4/IIIB cells. Inhibition of virus adsorption to the host cells was measured by a p24 antigen capture enzyme-linked immunosorbent assay. RESULTS: DS-4152 showed potent and selective inhibition of HIV-1 replication in the cell systems. Its 50% effective concentration for HIV-1 (IIIB strain) in MT-4 cells was 0.7 microgram/ml. The compound was not cytotoxic at concentrations < or = 100 micrograms/ml. DS-4125 proved inhibitory to syncytium-formation and virus adsorption. The anti-HIV-1 activities of zidovudine, dideoxycytidine and dideoxyinosine were not affected by the presence of DS-4152. CONCLUSION: DS-4152 has the potential, from these in vitro studies, to function as an anti-HIV-1 as well as an anti-angiogenesis agent. In order to determine this possibility, consequences of DS-4152 infusion on HIV-1 p24 serum levels and CD4+ cell counts over time are being examined in ongoing clinical trials in the United States on patients with AIDS-associated KS.

L13 ANSWER 14 OF 16 MEDLINE on STN
AB In vitro and in vivo model systems for the study of human immunodeficiency virus (HIV)-associated Kaposi's sarcoma (KS) were used to evaluate compounds for their potential as therapeutic agents. A sulfated polysaccharide-peptidoglycan compound (SP-PG) produced by bacteria controlled the in vitro growth of acquired immunodeficiency syndrome (AIDS)-associated, KS-derived spindle-shaped cells (AIDS-KS cells) at noncytotoxic concentrations. Angiogenesis induced by AIDS-KS cells in the chicken chorioallantoic membrane assay was blocked by SP-PG, which also inhibited the vascular hyperpermeability response and the angiogenesis associated with the induction of KS-like lesions that develop after subcutaneous inoculation of AIDS-KS cells into nude mice. Suramin, pentosan polysulfate, and interferon alpha, which are currently in use for therapy of KS, were either less effective than SP-PG or much more cytotoxic, or both.

L13 ANSWER 15 OF 16 MEDLINE on STN
AB Neovascularization is critical for the growth of tumours and is a dominant feature in a variety of angiogenic diseases such as diabetic retinopathy, haemangiomas, arthritis and psoriasis. Recognition of the

potential therapeutic benefit of controlling unabated capillary growth has led to a search for safe and effective angiogenesis inhibitors. We report here the synthesis of a family of novel inhibitors that are analogues of fumagillin, a naturally secreted antibiotic of Aspergillus fumigatus fresenius. We first isolated this fungus from a contaminated culture of capillary endothelial cells. Purified fumagillin inhibited endothelial cell proliferation in vitro and tumour-induced angiogenesis in vivo; it also inhibited tumour growth in mice, but prolonged administration was limited because it caused severe weight loss. Synthesis of fumagillin analogues yielded potent angiogenesis inhibitors ('angioinhibins') which suppress the growth of a wide variety of tumours with relatively few side-effects.

=> d 1-16

L13 ANSWER 1 OF 16 MEDLINE on STN
AN 2007248794 MEDLINE
DN PubMed ID: 17127716
TI Biological assays and genomic analysis reveal lipoic acid modulation of endothelial cell behavior and gene expression.
AU Larghero Patrizia; Vene Roberta; Minghelli Simona; Travaini Giorgia; Morini Monica; Ferrari Nicoletta; Pfeffer Ulrich; Noonan Douglas M; Albini Adriana; Benelli Roberto
CS Centro di Biotecnologie Avanzate, Genova, Italy.
SO Carcinogenesis, (2007 May) Vol. 28, No. 5, pp. 1008-20. Electronic Publication: 2006-11-24.
Journal code: 8008055. ISSN: 0143-3334.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200707
ED Entered STN: 27 Apr 2007
Last Updated on STN: 10 Jul 2007
Entered Medline: 9 Jul 2007

L13 ANSWER 2 OF 16 MEDLINE on STN
AN 2004546227 MEDLINE
DN PubMed ID: 15517885
TI Role of resveratrol in prevention and therapy of cancer: preclinical and clinical studies.
AU Aggarwal Bharat B; Bhardwaj Anjana; Aggarwal Rishi S; Seeram Navindra P; Shishodia Shishir; Takada Yasunari
CS Cytokine Research Laboratory, Department of Bioimmunotherapy, The University of Texas M. D. Anderson Cancer Center, Box 143, 1515 Holcombe Boulevard, Houston, Texas 77030, USA.. aggarwal@mdanderson.org
NC P01 CA91844 (NCI)
SO Anticancer research, (2004 Sep-Oct) Vol. 24, No. 5A, pp. 2783-840. Ref: 370
Journal code: 8102988. ISSN: 0250-7005.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200412
ED Entered STN: 3 Nov 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 10 Dec 2004

L13 ANSWER 3 OF 16 MEDLINE on STN
AN 2001572154 MEDLINE
DN PubMed ID: 11678646
TI Effect of HGF-like basic hexapeptides on angiogenesis.
AU Fazekas K; Janovics A; Dome B; Koska P; Albini A; Timar J
CS Department of Tumor Progression, National Institute of Oncology, Budapest, H-1122, Hungary.
SO Microvascular research, (2001 Nov) Vol. 62, No. 3, pp. 440-4.
Journal code: 0165035. ISSN: 0026-2862.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200201
ED Entered STN: 29 Oct 2001
Last Updated on STN: 1 Feb 2002
Entered Medline: 31 Jan 2002

L13 ANSWER 4 OF 16 MEDLINE on STN
AN 2001082166 MEDLINE
DN PubMed ID: 11060750
TI TNP-470: an angiogenesis inhibitor in clinical development for cancer.
AU Kruger E A; Figg W D
CS National Cancer Institute/NIH, Medicine Branch, 9000 Rockville Pike, Bethesda, MD 20892, USA.
SO Expert opinion on investigational drugs, (2000 Jun) Vol. 9, No. 6, pp. 1383-96. Ref: 100
Journal code: 9434197. ISSN: 1354-3784.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 8 Jan 2001

L13 ANSWER 5 OF 16 MEDLINE on STN
AN 2001011220 MEDLINE
DN PubMed ID: 10946555
TI Antitumor effect of the angiogenesis inhibitor, TNP470, on squamous cell carcinoma cells in head and neck cancer.
AU Kawano T; Furukawa S; Matsuda H; Takahashi M; Endo R; Inoue M; Nishimura G; Tsukuda M
CS Department of Otorhinolaryngology, Yokohama City Medical Center Hospital.
SO Nippon Jibiinkoka Gakkai kaiho, (2000 Jul) Vol. 103, No. 7, pp. 821-8.
Journal code: 7505728. ISSN: 0030-6622.
CY Japan
DT (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 200010
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 26 Oct 2000

L13 ANSWER 6 OF 16 MEDLINE on STN
AN 1999437797 MEDLINE
DN PubMed ID: 10508038

TI Anti-Kaposi's sarcoma and antiangiogenic activities of sulfated dextrins.
AU Thornton M; Barkley L; Mason J C; Shaunak S
CS Departments of Infectious Diseases, Imperial College School of Medicine, Hammersmith Hospital, London, United Kingdom.
SO Antimicrobial agents and chemotherapy, (1999 Oct) Vol. 43, No. 10, pp. 2528-33.
Journal code: 0315061. ISSN: 0066-4804.
CY United States
DT (CASE REPORTS)
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals; AIDS
EM 199912
ED Entered STN: 13 Jan 2000
Last Updated on STN: 13 Jan 2000
Entered Medline: 13 Dec 1999

L13 ANSWER 7 OF 16 MEDLINE on STN
AN 1998369539 MEDLINE
DN PubMed ID: 9703916
TI Angiogenic inhibition for the treatment of head and neck cancer.
AU Gleich L L; Zimmerman N; Wang Y O; Gluckman J L
CS Department of Otolaryngology-Head and Neck Surgery, University of Cincinnati Medical Center, Ohio, USA.
SO Anticancer research, (1998 Jul-Aug) Vol. 18, No. 4A, pp. 2607-9.
Journal code: 8102988. ISSN: 0250-7005.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 10 Sep 1998
Last Updated on STN: 10 Sep 1998
Entered Medline: 1 Sep 1998

L13 ANSWER 8 OF 16 MEDLINE on STN
AN 1998211776 MEDLINE
DN PubMed ID: 9552050
TI Fumagillin analog in the treatment of Kaposi's sarcoma: a phase I AIDS Clinical Trial Group study. AIDS Clinical Trial Group Number 215 Team.
AU Dezube B J; Von Roenn J H; Holden-Wiltse J; Cheung T W; Remick S C; Cooley T P; Moore J; Sommadossi J P; Shriver S L; Suckow C W; Gill P S
CS Beth Israel Deaconess Medical Center, Boston, MA, USA.
NC AI25915 (NIAID)
AI27659 (NIAID)
AI27667 (NIAID)
+
SO Journal of clinical oncology : official journal of the American Society of Clinical Oncology, (1998 Apr) Vol. 16, No. 4, pp. 1444-9.
Journal code: 8309333. ISSN: 0732-183X.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals; AIDS
EM 199805

ED Entered STN: 20 May 1998
Last Updated on STN: 20 May 1998
Entered Medline: 12 May 1998

L13 ANSWER 9 OF 16 MEDLINE on STN
AN 97170239 MEDLINE
DN PubMed ID: 9017768
TI The pharmacokinetics of TNP-470, a new angiogenesis inhibitor.
AU Figg W D; Pluda J M; Lush R M; Saville M W; Wyvill K; Reed E; Yarchoan R
CS Clinical Pharmacokinetics Section, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
SO Pharmacotherapy, (1997 Jan-Feb) Vol. 17, No. 1, pp. 91-7.
Journal code: 8111305. ISSN: 0277-0008.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LA English
FS Priority Journals; AIDS
EM 199704
ED Entered STN: 22 Apr 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 8 Apr 1997

L13 ANSWER 10 OF 16 MEDLINE on STN
AN 96437090 MEDLINE
DN PubMed ID: 8839904
TI A phase I clinical and pharmacokinetic study of the angiogenesis inhibitor, tecogalan sodium.
AU Eckhardt S G; Burris H A; Eckardt J R; Weiss G; Rodriguez G; Rothenberg M; Rinaldi D; Barrington R; Kuhn J G; Masuo K; Sudo K; Atsumi R; Oguma T; Higashi L; Fields S; Smetzer L; Von Hoff D D
CS Cancer Therapy and Research Center, University of Texas Health Science Center at San Antonio, USA.
SO Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, (1996 Jul) Vol. 7, No. 5, pp. 491-6.
Journal code: 9007735. ISSN: 0923-7534.
CY Netherlands
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 28 Jan 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 26 Dec 1996

L13 ANSWER 11 OF 16 MEDLINE on STN
AN 96249989 MEDLINE
DN PubMed ID: 8927305
TI Tecogalan sodium inhibits corneal neovascularization induced by basic fibroblast growth factor.
AU Murata T; Ishibashi T; Yoshikawa H; Khalil A; Inomata H
CS Department of Ophthalmology, Faculty of Medicine, Kyushu University, Fukuoka, Japan.
SO Ophthalmic research, (1995) Vol. 27, No. 6, pp. 330-4.
Journal code: 0267442. ISSN: 0030-3747.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199611
ED Entered STN: 19 Dec 1996
Last Updated on STN: 19 Dec 1996
Entered Medline: 14 Nov 1996

L13 ANSWER 12 OF 16 MEDLINE on STN
AN 95257086 MEDLINE
DN PubMed ID: 7738759
TI Treatment of murine hemangioendotheliomas with the angiogenesis inhibitor AGM-1470.
AU O'Reilly M S; Brem H; Folkman J
CS Department of Surgery, Children's Hospital, Boston, MA 02115, USA.
NC CA-37395-08 (NCI)
SO Journal of pediatric surgery, (1995 Feb) Vol. 30, No. 2, pp. 325-9; discussion 329-30.
Journal code: 0052631. ISSN: 0022-3468.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 15 Jun 1995
Last Updated on STN: 3 Feb 1997
Entered Medline: 7 Jun 1995

L13 ANSWER 13 OF 16 MEDLINE on STN
AN 94280703 MEDLINE
DN PubMed ID: 7516666
TI Anti-angiogenesis agent DS-4152 is a potent and selective inhibitor of HIV-1 replication in vitro.
AU Baba M; Shigeta S; Ikeuchi T; Korenaga H; Osada Y
CS Department of Microbiology, Fukushima Medical College, Japan.
SO AIDS (London, England), (1994 Jan) Vol. 8, No. 1, pp. 43-8.
Journal code: 8710219. ISSN: 0269-9370.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals; AIDS
EM 199407
ED Entered STN: 10 Aug 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 26 Jul 1994

L13 ANSWER 14 OF 16 MEDLINE on STN
AN 92179712 MEDLINE
DN PubMed ID: 1371891
TI Inhibition of development of Kaposi's sarcoma-related lesions by a bacterial cell wall complex.
AU Nakamura S; Sakurada S; Salahuddin S Z; Osada Y; Tanaka N G; Sakamoto N; Sekiguchi M; Gallo R C
CS Department of Internal Medicine, University of Southern California, Los Angeles 90033.
SO Science (New York, N.Y.), (1992 Mar 13) Vol. 255, No. 5050, pp. 1437-40.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199204
ED Entered STN: 24 Apr 1992

Last Updated on STN: 6 Feb 1998
Entered Medline: 8 Apr 1992

L13 ANSWER 15 OF 16 MEDLINE on STN
AN 91061914 MEDLINE
DN PubMed ID: 1701033
TI Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumour growth.
AU Ingber D; Fujita T; Kishimoto S; Sudo K; Kanamaru T; Brem H; Folkman J
CS Department of Surgery, Children's Hospital, Boston, Massachusetts.
SO Nature, (1990 Dec 6) Vol. 348, No. 6301, pp. 555-7.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals; Space Life Sciences
EM 199101
ED Entered STN: 22 Feb 1991
Last Updated on STN: 29 Jan 1996
Entered Medline: 10 Jan 1991

L13 ANSWER 16 OF 16 MEDLINE on STN
AN 90100565 MEDLINE
DN PubMed ID: 1688470
TI Inhibition of angiogenesis by recombinant human platelet factor-4 and related peptides.
AU Maione T E; Gray G S; Petro J; Hunt A J; Donner A L; Bauer S I; Carson H F; Sharpe R J
CS Repligen Corporation, Cambridge, MA 02139.
SO Science (New York, N.Y.), (1990 Jan 5) Vol. 247, No. 4938, pp. 77-9.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199002
ED Entered STN: 28 Mar 1990
Last Updated on STN: 29 Jan 1996
Entered Medline: 5 Feb 1990

=> s lymphangiogenesis or (Sturge(w) Weber) or (verruca(w) vulgaris) or (tuberous(w)sclerosis) or eczema or (molluscum(w)contagious) or (seborrheic(w)keratosis) or (actinic(w)keratosis)
646 LYMPHANGIOGENESIS
1107 STURGE
4948 WEBER
1096 STURGE(W) WEBER
763 VERRUCA
21873 VULGARIS
238 VERRUCA(W) VULGARIS
5058 TUBEROUS
70885 SCLEROSIS
4613 TUBEROUS(W)SCLEROSIS
12662 ECZEMA
1299 MOLLUSCUM
3154 CONTAGIOUS
1 MOLLUSCUM(W)CONTAGIOUS
2969 SEBORRHEIC
8273 KERATOSIS
379 SEBORRHEIC(W)KERATOSIS

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          2632 ACTINIC
          8273 KERATOSIS
           598 ACTINIC(W)KERATOSIS
L14      20067 LYMPHANGIOGENESIS OR (STURGE(W) WEBER) OR (VERRUCA(W) VULGARIS)
               OR (TUBEROUS(W)SCLEROSIS) OR ECZEMA OR (MOLLUSCUM(W)CONTAGIOUS)
              OR (SEBORRHEIC(W)KERATOSIS) OR (ACTINIC(W)KERATOSIS)

=> s l4 and l2
L15        926 L4 AND L2

=> d his

     (FILE 'HOME' ENTERED AT 12:14:57 ON 16 JUL 2007)

     FILE 'MEDLINE' ENTERED AT 12:15:09 ON 16 JUL 2007
L1       56469 S ANGIOSARCOMA OR HEMANGIOENDOTHELIOMA OR (BASAL (W) CELL(W)CAR
L2       30688 S ANGIOGENESIS
L3         702 S L1 AND L2
L4       71291 S KAPOSI? OR PSORIASIS OR LYMPHANGIOGENESIS OR HEMANGIOMA OR (S
L5         926 S L4 AND L2
L6       12978 S (RECESSIVE(W)DYSTROPHIC (W)EPIDERMOLYSIS(W)BULLOSA) OR (VENOU
L7          32 S L6 AND L2
L8        1951 S CURCUMIN
L9           5 S L8 AND (L3 OR L5 OR L7)
L10        281 S (COLLAGENASE(W)INHIBITO?)
L11          1 S L10 AND (L3 OR L5 OR L7)
L12       7932 S FUMAGILLIN OR SULFATED OR AMINOPHENYLPHOSPHONIC OR OXINDOLE
L13         16 S L12 AND (L3 OR L5 OR L7)
L14      20067 S LYMPHANGIOGENESIS OR (STURGE(W) WEBER) OR (VERRUCA(W) VULGARI
L15        926 S L4 AND L2

=> s l10 and l15
L16          1 L10 AND L15

=> d

L16  ANSWER 1 OF 1     MEDLINE on STN
AN   95101158     MEDLINE
DN   PubMed ID: 7528513
TI   Angiogenic potential in vivo by Kaposi's sarcoma cell-free
     supernatants and HIV-1 tat product: inhibition of KS-like lesions by
     tissue inhibitor of metalloproteinase-2.
AU   Albini A; Fontanini G; Masiello L; Tacchetti C; Bigini D; Luzzi P; Noonan
     D M; Stetler-Stevenson W G
CS   National Institute of Research on Cancer, Genoa, Italy.
SO   AIDS (London, England), (1994 Sep) Vol. 8, No. 9, pp. 1237-44.
     Journal code: 8710219. ISSN: 0269-9370.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA   English
FS   Priority Journals; AIDS
EM   199501
ED   Entered STN: 15 Feb 1995
     Last Updated on STN: 3 Mar 2000
     Entered Medline: 30 Jan 1995


=> d ab

L16  ANSWER 1 OF 1     MEDLINE on STN
AB   OBJECTIVE: To determine the neoplastic nature of Kaposi's
     sarcoma (KS).  A highly vascularized lesion, KS is frequently associated
     with AIDS, indicating HIV products may be involved.  DESIGN AND METHODS:
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We determined the angiogenic properties of KS cell-secreted products and the HIV-1-tat gene product in vivo. Cell-free secreted products (KS-CM) from cultured epidemic and sporadic KS spindle cells or recombinant (r) HIV-1 tat protein were injected into mice with a matrix support (Matrigel). RESULTS: KS-CM produced lesions carrying all the phenotypic hallmarks of KS, as observed by light and electron microscopy: spindle-shaped cells, haemorrhages and an inflammatory infiltrate, as well as Factor VIII-positive endothelial cells lining new blood vessels. Electron microscopy indicated an initial granulocyte invasion, with spindle-cell migration and neocapillary formation in the centre of the matrix. These lesions required the cofactor heparin; KS-CM or heparin alone were poorly angiogenic. A less intense angiogenesis, with lower cellularity and few granulocytes, was observed in basic fibroblast growth factor (bFGF)/heparin lesions, indicating that factors other than bFGF are present in the KS spindle-cell products. When the collagenase inhibitor tissue inhibitor of metalloproteinases (TIMP)-2 was added to the sponges, KS-CM-induced angiogenesis was reduced by approximately 65% and bFGF-induced angiogenesis inhibited completely. Recombinant HIV-1 tat protein, a growth factor for KS cells, induced vascularization that was also enhanced by heparin, implying that HIV-1 tat could contribute to the aetiology of HIV-associated KS. CONCLUSIONS: KS-like lesions were obtained by injecting cell-free secreted products, suggesting that KS is a 'self-propagating' proliferative lesion caused by a cytokine imbalance and not a true neoplasm. Heparin-binding factors appear to be involved, and HIV-1 tat angiogenic properties implicate this molecule in AIDS-associated KS. Inhibition of KS-CM-induced KS-like lesions by TIMP-2 suggests that metalloproteinase inhibitors could be potential therapeutic agents for KS.

=> d kwic

L16 ANSWER 1 OF 1 MEDLINE on STN
TI Angiogenic potential in vivo by Kaposi's sarcoma cell-free supernatants and HIV-1 tat product: inhibition of KS-like lesions by tissue inhibitor of metalloproteinase-2.
AB OBJECTIVE: To determine the neoplastic nature of Kaposi's sarcoma (KS). A highly vascularized lesion, KS is frequently associated with AIDS, indicating HIV products may be involved. DESIGN AND. . . centre of the matrix. These lesions required the cofactor heparin; KS-CM or heparin alone were poorly angiogenic. A less intense angiogenesis, with lower cellularity and few granulocytes, was observed in basic fibroblast growth factor (bFGF)/heparin lesions, indicating that factors other than bFGF are present in the KS spindle-cell products. When the collagenase inhibitor tissue inhibitor of metalloproteinases (TIMP)-2 was added to the sponges, KS-CM-induced angiogenesis was reduced by approximately 65% and bFGF-induced angiogenesis inhibited completely. Recombinant HIV-1 tat protein, a growth factor for KS cells, induced vascularization that was also enhanced by heparin,. . .
CT . . .
inhibitors
Mice
Mice, Inbred C57BL
Mice, Nude
Microscopy, Electron
*Neovascularization, Pathologic: ET, etiology
Neovascularization, Pathologic: PA, pathology
Proteins: PD, pharmacology
*Sarcoma, Kaposi: ET, etiology
Sarcoma, Kaposi: PA, pathology
Sarcoma, Kaposi: PC, prevention & control
Tissue Inhibitor of Metalloproteinase-2

```
=> s l14 and l2
L17         280 L14 AND L2

=> s l17 and l10
L18           0 L17 AND L10

=> s inhibit? and l17
       1351819 INHIBIT?
L19          79 INHIBIT? AND L17

=> d ab 1-5

L19  ANSWER 1 OF 79     MEDLINE on STN
AB   The interaction between endothelial cells and extracellular matrix
     proteins plays an important role in (hem)angiogenesis.
     Integrins are able to mediate the outgrowth of newly formed blood vessels.
     In contrast, the role of integrins in lymphangiogenesis, ie, the
     outgrowth of new from pre-existing lymphatic vessels, has so far been
     unclear.  Here, expression and functional relevance of integrins on
     lymphatic endothelium in vivo was investigated using the mouse model of
     combined inflammatory corneal hemangiogenesis and
     lymphangiogenesis.  Immunohistochemistry revealed novel expression
     of both integrin alpha5 and alphav on both resting and activated lymphatic
     vessels in vivo.  Integrin alpha5-inhibiting small molecules
     significantly blocked the outgrowth of new lymphatic vessels into the
     cornea in a dose-dependent manner.  The outgrowth of blood vessels was
     less significantly affected by this treatment, thus allowing for selective
     inhibition of lymphangiogenesis at lower dosages.
     Combined inhibition of integrin alpha5 and alphav using
     inhibiting molecules did not significantly increase the
     anti-lymphangiogenic effect in vivo, thus suggesting an important
     functional role of integrin alpha5 in lymphangiogenesis.  In
     summary, our findings demonstrate novel expression of specific integrins
     on growing lymphatic endothelial cells in vivo and reveal their functional
     role during lymphangiogenesis.  This opens new treatment options
     for selective inhibition of lymphangiogenesis, eg, in
     oncology and transplant immunology.

L19  ANSWER 2 OF 79     MEDLINE on STN
AB   PURPOSE: To analyze whether bevacizumab can inhibit inflammatory
     angiogenesis and lymphangiogenesis in the cornea.
     Bevacizumab (Avastin; Roche, Welwyn Garden City, UK) is a recombinant,
     humanized, monoclonal antibody against VEGF-A that has been approved by
     the U.S.  Food and Drug Administration for the treatment of colon
     carcinomas.  METHODS: The mouse model of suture-induced corneal
     neovascularization was used to assess the antihemangiogenic and
     antilymphangiogenic effect of bevacizumab by systemic and topical
     application.  Corneal flatmounts were stained with LYVE-1 as a specific
     lymphatic vascular endothelial marker and CD31 as a pan-endothelial
     marker, and blood and lymph vascularized areas were analyzed
     morphometrically.  The inhibitory effect of bevacizumab on
     lymphatic endothelial cells (LECs) was analyzed with a colorimetric (BrdU)
     proliferation ELISA.  The binding ability of bevacizumab to murine VEGF-A
     was analyzed by Western blot, ELISA, and surface plasmon resonance.
     RESULTS: The systemic and topical applications of bevacizumab
     significantly inhibited the outgrowth of blood (P < 0.006 and P
     < 0.0001, respectively) and lymphatic (P < 0.002 and P < 0.0001,
     respectively) vessels.  Inhibition of the proliferation of LECs
     was also significant (P < 0.0001).  Western blot analysis, ELISA, and the
     surface plasmon resonance assay showed that bevacizumab binds murine
     VEGF-A.  CONCLUSIONS: Topical or systemic application of bevacizumab
     inhibits both inflammation-induced angiogenesis and
     lymphangiogenesis in the cornea.  This finding suggests an
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important role of VEGF-A in corneal lymphangiogenesis.
Bevacizumab may be useful in preventing immune rejections after
penetrating keratoplasty or tumor metastasis via lymphatic vessels.

L19 ANSWER 3 OF 79 MEDLINE on STN
AB Inflammation occurs in response to host injury or infection, as the result of an autoimmune disease, or in response to the development of a tumor. Although the immune system may be helpful in fighting the tumor, it may also fuel the tumorigenic process. In fact, recent data suggest a strong link between chronic inflammation, angiogenesis, and the development of cancer. For example, inflammation and scarring caused by recurring infections with Mycobacterium tuberculosis may be a cause for cancers of the lung. Inflammatory breast cancer exhibits increased angiogenesis and lymphangiogenesis and has a higher metastatic potential than noninflammatory breast cancer. Nonsteroidal anti-inflammatory drugs have been proposed as preventives for the development of colon carcinoma and ovarian cancer. Inhibition of nuclear factor-kappaB contributes to the proposed mechanism of action. Inflammatory cytokines, including interleukin-6, serve as autocrine and paracrine growth factors for several cancers, and high levels of these cytokines may correlate with a poor prognosis and increased production of angiogenic factors. The state of the art of our understanding of this critical interaction is reviewed.

L19 ANSWER 4 OF 79 MEDLINE on STN
AB Vascular endothelial growth factor A (VEGF-A) is a potent inducer of angiogenesis. We now show that VEGF-A-induced adhesion and migration of human endothelial cells are dependent on the integrin alpha9beta1 and that VEGF-A is a direct ligand for this integrin. Adhesion and migration of these cells on the 165 and 121 isoforms of VEGF-A depend on cooperative input from alpha9beta1 and the cognate receptor for VEGF-A, VEGF receptor 2 (VEGF-R2). Unlike alpha3beta1or alphavbeta3 integrins, alpha9beta1 was also found to bind the 121 isoform of VEGF-A. This interaction appears to be biologically significant, because alpha9beta1-blocking antibody dramatically and specifically inhibited angiogenesis induced by VEGF-A165 or -121.
Together with our previous findings that alpha9beta1 directly binds to VEGF-C and -D and contributes to lymphangiogenesis, these results identify the integrin alpha9beta1 as a potential pharmacotherapeutic target for inhibition of pathogenic angiogenesis and lymphangiogenesis.

L19 ANSWER 5 OF 79 MEDLINE on STN

=> s (Sturge(w) Weber) or (verruca(w) vulgaris) or (tuberous(w)sclerosis) or eczema or (molluscum(w)contagious) or (seborrheic(w)keratosis) or (actinic(w)keratosis)

1107	STURGE
4948	WEBER
1096	STURGE(W) WEBER
763	VERRUCA
21873	VULGARIS
238	VERRUCA(W) VULGARIS
5058	TUBEROUS
70885	SCLEROSIS
4613	TUBEROUS(W)SCLEROSIS
12662	ECZEMA
1299	MOLLUSCUM
3154	CONTAGIOUS
1	MOLLUSCUM(W)CONTAGIOUS
2969	SEBORRHEIC
8273	KERATOSIS
379	SEBORRHEIC(W)KERATOSIS
2632	ACTINIC

```
          8273 KERATOSIS
           598 ACTINIC(W)KERATOSIS
L20      19423 (STURGE(W) WEBER) OR (VERRUCA(W) VULGARIS) OR (TUBEROUS(W)SCLERO
               SIS) OR ECZEMA OR (MOLLUSCUM(W)CONTAGIOUS) OR (SEBORRHEIC(W)KERA
              TOSIS) OR (ACTINIC(W)KERATOSIS)

=> d his

     (FILE 'HOME' ENTERED AT 12:14:57 ON 16 JUL 2007)

     FILE 'MEDLINE' ENTERED AT 12:15:09 ON 16 JUL 2007
L1        56469 S ANGIOSARCOMA OR HEMANGIOENDOTHELIOMA OR (BASAL (W) CELL(W)CAR
L2        30688 S ANGIOGENESIS
L3          702 S L1 AND L2
L4        71291 S KAPOSI? OR PSORIASIS OR LYMPHANGIOGENESIS OR HEMANGIOMA OR (S
L5          926 S L4 AND L2
L6        12978 S (RECESSIVE(W)DYSTROPHIC (W)EPIDERMOLYSIS(W)BULLOSA) OR (VENOU
L7           32 S L6 AND L2
L8         1951 S CURCUMIN
L9            5 S L8 AND (L3 OR L5 OR L7)
L10         281 S (COLLAGENASE(W)INHIBITO?)
L11           1 S L10 AND (L3 OR L5 OR L7)
L12        7932 S FUMAGILLIN OR SULFATED OR AMINOPHENYLPHOSPHONIC OR OXINDOLE
L13          16 S L12 AND (L3 OR L5 OR L7)
L14       20067 S LYMPHANGIOGENESIS OR (STURGE(W) WEBER) OR (VERRUCA(W) VULGARI
L15         926 S L4 AND L2
L16           1 S L10 AND L15
L17         280 S L14 AND L2
L18           0 S L17 AND L10
L19          79 S INHIBIT? AND L17
L20       19423 S (STURGE(W) WEBER) OR (VERRUCA(W) VULGARIS) OR (TUBEROUS(W)SCL
=> s l20 and l2
L21          24 L20 AND L2

=> d ab 1-24

L21  ANSWER 1 OF 24      MEDLINE on STN
AB   Cutaneous and leptomeningeal vascular malformations are hallmarks of the
     Sturge-Weber Syndrome (SWS), resulting in chronic
     ischemic tissue damage.  The mechanisms underlying the pathobiology of
     these progressive lesions are unknown.  Aberrant expression of angiogenic
     factors has been implicated in the genesis and maintenance of vascular
     malformations.  To assess the role of angiogenesis in SWS
     vascular lesions we determined the expression of key angiogenic factors by
     immunohistochemistry and in situ hybridization in 8 SWS patients (age: 8
     months to 18 years).  We observed increased expression of vascular
     endothelial growth factor (VEGF), its cognate receptors VEGFR-1, VEGFR-2,
     and neuropilin (NP)-1 as well as Tie2 in leptomeningeal SWS blood vessels.
     Intriguingly, these factors are known to be transcriptionally induced by
     hypoxia-inducible factor (HIF).  The HIF system has emerged as the key
     regulatory system of responses to hypoxia.  Immunohistochemical analysis
     demonstrated markedly elevated nuclear HIF-1alpha and HIF-2alpha protein
     levels in SWS vessels.  Concomitantly, SWS vessels revealed signs of
     enhanced endothelial cell (EC) turnover as evidenced by increased EC
     proliferation and apoptosis.  Thus, in terms of angiogenesis,
     vascular malformations in SWS are not static lesions but constitute
     dynamic structures.  Our observation of a dysregulated HIF-alpha
     expression in SWS vessels are in agreement with recent findings that
     EC-specific HIF activation provides a setting which supports and sustains
     angiogenesis and could be of potential use for developing
     therapeutic strategies to treat these currently incurable lesions.

L21  ANSWER 2 OF 24      MEDLINE on STN
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AB A central regulator of cell growth that has been implicated in responses to stress such as hypoxia is mTOR (mammalian Target Of Rapamycin). We have shown previously that mTOR is required for angiogenesis in vitro and endothelial cell proliferation in response to hypoxia. Here we have investigated mTOR-associated signaling components under hypoxia and their effects on cell proliferation in rat aortic endothelial cells (RAECs). Hypoxia (1% O(2)) rapidly (>30 minutes) and in a concentration-dependent manner promoted rapamycin-sensitive and sustained phosphorylation of mTOR-Ser2448 followed by nuclear translocation in RAECs. Similarly, hypoxia induced phosphorylation of the mTORC2 substrate Akt-Ser473 (3 to 6 hours at 1% O(2)) and a brief phosphorylation peak of the mTORC1 substrate S6 kinase-Thr389 (10 to 60 minutes). Phosphorylation of Akt was inhibited by mTOR knockdown and partially with rapamycin. mTOR knockdown, rapamycin, or Akt inhibition specifically and significantly inhibited proliferation of serum-starved RAECs under hypoxia ($P<0.05$; n> or =4). Similarly, hypoxia induced Akt-dependent and rapamycin-sensitive proliferation in mouse embryonic fibroblasts. This response was partially blunted by hypoxia-inducible factor-1alpha knockdown and not affected by TSC2 knockout. Finally, mTORC2 inhibition by rictor silencing, especially ($P<0.001$; n=7), and mTORC1 inhibition by raptor silencing, partially ($P<0.05$; n=7), inhibited hypoxia-induced RAEC proliferation. Thus, mTOR mediates an early response to hypoxia via mTORC1 followed by mTORC2, promoting endothelial proliferation mainly via Akt signaling. mTORC1 and especially mTORC2 might therefore play important roles in diseases associated with hypoxia and altered angiogenesis.

L21 ANSWER 3 OF 24 MEDLINE on STN

AB The Ras-Raf-MEK-ERK signalling pathway is frequently dysregulated in human malignancies, as is angiogenesis and the vascular endothelial growth factor receptor (VEGF/VEGFR) pathway. These kinases are therefore important anticancer targets. The novel, oral treatment sorafenib (BAY 43-9006), has been shown to be an inhibitor of VEGFR, Raf and platelet-derived growth factor in clinical trials against a variety of cancers, with the greatest activity to date observed in metastatic renal cancer. Although side-effects with this targeted therapy are usually not dose-limiting, they frequently involve the skin, and consist of a maculopapular rash, palmar-plantar dysaesthesia, alopecia and xerosis. In this report, we present two patients in whom treatment with sorafenib resulted in inflammation of actinic keratosis, which in some cases progressed to invasive squamous cell carcinoma. This side-effect is of clinical importance, as early recognition is critical for early treatment and may represent a source of additional morbidity to these patients.

L21 ANSWER 4 OF 24 MEDLINE on STN

AB This vascular review is organized under the following headings: vasculogenesis and angiogenesis; vascular endothelial growth factors, their receptors, TIE receptors, and angiopoietins; other factors in blood vessel formation; parallel patterning in blood vessels and nerves; physiological and pathological neovascularization; the role of VEGF receptors in metastasis; anti-angiogenic therapy for tumors; association of blood vessels with fat; vascular malformations and vascular tumors; infantile hemangiomas; congenital hemangiomas; lymphatic malformations; molecular characteristics of some disorders with vascular malformations; Kasabach-Merritt phenomenon; Sturge-Weber syndrome, Klippel-Trenaunay syndrome, and Parkes Weber syndrome; diagnostic and laboratory studies; and future perspectives.

L21 ANSWER 5 OF 24 MEDLINE on STN

AB New oncogenes and tumor suppressor genes that play an important role in the pathogenesis of urothelial bladder carcinoma have been discovered. The objectives of this review were to summarize the most important oncogenes and tumor suppressor genes involved in urothelial carcinoma and to address their role in pathogenesis, their prognostic value, and their

potential use as therapeutic targets. The collected data led the authors to propose a common pathway in which the fibroblastic growth factor receptor 3 (FGFR3) mutation seems to be the earliest genetic abnormality responsible for the transformation from normal tissue to atypia and dysplasia. Three different progression pathways were proposed: The first operative pathway is from dysplasia to superficial papillary pathologic Ta (pTa) tumors to pT1 tumors and, ultimately, to pT2 tumors with FGFR3 and tuberous sclerosis complex 1 (TSC1) the responsible genes. The second major operative pathway is from dysplasia, to carcinoma in situ, and to solid pT1 and pT2 tumors. The third pathway of progression is from dysplasia to papillary T1 and pT2 tumors. The genes involved in the last 2 pathways are the p53, serine threonine protein kinase 15 (STK15), triple-function domain (TRIO), fragile histidine triad (FHIT), p63 genes; and alterations of 20q and 5p, alterations of adhesions, angiogenesis, and matrix-remodeling gene products also are involved. Finally, murine leukemia viral oncogene homologue 1 (RAF1) and CD9 are involved in the progression from papillary pT1 tumors to pT2 tumors.

L21 ANSWER 6 OF 24 MEDLINE on STN
AB Imiquimod (imidazoquinoline 5%) is a topical immune response modifier agent that inhibits angiogenesis, the growth of new blood vessels. In addition to its stimulation of cell-mediated immunity, imiquimod's antiangiogenic activity contributes to its clinical efficacy by interfering with pathological neovascularization that promotes disease progression. The antiangiogenic mechanisms of imiquimod are due to its: 1) induction of cytokines that themselves inhibit angiogenesis (interferons, IL-10, IL-12); 2) local up-regulation of endogenous angiogenesis inhibitors (TIMP, TSP-1); 3) local down-regulation of pro-angiogenic factors (bFGF, MMP-9); and 4) promotion of endothelial cell apoptosis. This report discusses these mechanisms and the rationale for imiquimod's use as an antiangiogenic agent. Key principles of antiangiogenic therapy are presented to describe how imiquimod may be applied in a well-tolerated fashion to treat a broad range of angiogenesis-dependent dermatological conditions, including actinic keratosis (AK), basal cell carcinoma (BCC), squamous cell carcinoma (SCC), lentigo maligna, hemangiomas, Kaposi's sarcoma, pyogenic granuloma, and external genital warts.

L21 ANSWER 7 OF 24 MEDLINE on STN
AB Sturge-Weber syndrome presents with vascular malformations of the brain, skin, and eye. Fibronectin has potent effects on angiogenesis, vessel remodeling, and vessel innervation density. To determine fibronectin expression in the blood vessels of Sturge-Weber syndrome brain and skin tissue and to quantify the density and circumference of Sturge-Weber syndrome blood vessels by type compared with controls, we performed in situ hybridization for fibronectin messenger ribonucleic acid (RNA) expression on six Sturge-Weber syndrome cortical brain samples, six epilepsy brain samples, skin from two port-wine stain skin lesions, and two normal skin samples from two subjects with Sturge -Weber syndrome. Fibronectin messenger RNA was expressed in blood vessels and endothelial cells in the parenchyma of both Sturge-Weber syndrome and control brain tissues and in skin samples. Fibronectin expression was significantly reduced by 23% in the Sturge-Weber syndrome meningeal vessels compared with the epilepsy controls ($P < .01$). Fibronectin expression was significantly increased by 19% in the Sturge-Weber syndrome parenchymal vessels compared with the epilepsy controls ($P < .05$). No difference was found in the expression of fibronectin in port-wine stain skin blood vessels. The density of leptomeningeal blood vessels in the Sturge-Weber syndrome brain tissue samples was 45% greater than in the epilepsy samples ($P < .05$). Blood

vessel circumference was significantly decreased in the Sturge-Weber syndrome meningeal vessels compared with the controls (27%; P < .05). When blood vessels from different brain regions were compared, fibronectin expression was decreased in Sturge-Weber syndrome meningeal vessels and was increased in the parenchymal vessels. Altered blood vessel fibronectin expression in Sturge-Weber syndrome could contribute to abnormal vascular structure and function in this disorder.

L21 ANSWER 8 OF 24 MEDLINE on STN

AB Patients with tuberous sclerosis complex (TSC) develop hamartomatous tumors showing loss of function of the tumor suppressor TSC1 (hamartin) or TSC2 (tuberin) and increased angiogenesis, fibrosis, and abundant mononuclear phagocytes. To identify soluble factors with potential roles in TSC tumorigenesis, we screened TSC skin tumor-derived cells for altered gene and protein expression. Fibroblast-like cells from 10 angiofibromas and five periungual fibromas produced higher levels of monocyte chemoattractant protein-1 (MCP-1) mRNA and protein than did fibroblasts from the same patient's normal skin. Conditioned medium from angiofibroma cells stimulated chemotaxis of a human monocytic cell line to a greater extent than conditioned medium from TSC fibroblasts, an effect blocked by neutralizing MCP-1-specific antibody. Overexpression of MCP-1 seems to be caused by loss of tuberin function because Eker rat embryonic fibroblasts null for Tsc2 (EEF Tsc2(-/-)) produced 28 times as much MCP-1 protein as did EEF Tsc2(+/+) cells; transient expression of WT but not mutant human TSC2 by EEF Tsc2(-/-) cells inhibited MCP-1 production; and pharmacological inhibition of the Rheb-mTOR pathway, which is hyperactivated after loss of TSC2, decreased MCP-1 production by EEF Tsc2(-/-) cells. Together these findings suggest that MCP-1 is an important paracrine factor for TSC tumorigenesis and may be a new therapeutic target.

L21 ANSWER 9 OF 24 MEDLINE on STN

AB BACKGROUND: Peroxisome proliferator-activated receptors (PPARs) mediate several functions that are of interest in carcinogenesis. Although PPARalpha, PPARbeta, and PPARgamma are expressed in multiple human, their expression has not been investigated in non-melanoma skin cancer. METHODS: We performed a retrospective paired immunohistochemical analysis of normal skin, actinic keratosis (AK), and squamous cell carcinoma (SCC) among 35 individuals. Specimens were considered PPAR immunoreactive when 1% or more of the tumor cells showed clear evidence of immunostaining. Cyclooxygenase-2 (COX-2) expression, the fraction of proliferating endothelial cells, and microvessel density were also evaluated in these samples. RESULTS: PPARalpha immunoreactivity was significantly less likely to occur in SCC and AK than in normal skin of each individual. In contrast to PPARalpha, PPARbeta appeared to be upregulated in (pre)malignant skin lesions. For each individual, the likelihood that normal skin, AK, or SCC was immunoreactive against PPARgamma was comparable. COX-2 immunopositivity was significantly associated with PPARbeta and PPARgamma immunoreactivity. No statistical differences were noted for the angiogenesis parameters and PPARalpha, PPARbeta, or PPARgamma expression, except that the microvessel density was significantly higher among PPARbeta-immunoreactive SCCs compared to that among immunonegative SCCs. CONCLUSION: Although further research is warranted, these results suggest that PPAR ligands such as fibrates and thiazolidinediones may have chemoprophylactic properties in skin carcinogenesis.

L21 ANSWER 10 OF 24 MEDLINE on STN

AB BACKGROUND: Cyclooxygenase (COX)-2 expression and tumour-induced angiogenesis appear to be increased in squamous cell carcinoma (SCC) of the skin. In other cancers, COX-2 is a pro-angiogenic factor. The association between angiogenesis and COX-2 has not been studied in skin cancer. OBJECTIVES: To assess the onset of increased

COX-2 expression and angiogenesis in the multistage carcinogenesis of SCC as well as the correlation between those two parameters. PATIENTS/METHODS: We performed a retrospective paired immunohistochemical analysis of normal skin, actinic keratosis (AK), Bowen's disease (BD) and SCC among 35 individuals. Specimens were considered COX-2 immunopositive when 5% or more of the tumour cells showed clear evidence of immunostaining. To quantify active angiogenesis, we used a Ki-67-CD34 double-labelling immunohistochemical stain and calculated the fraction of proliferating endothelial cells. The Chalkley method was used to determine the microvessel density. To detect hypoxia, a carboanhydrase IX immunostain was used. RESULTS: Compared with normal epidermis (0%), AK (31%), BD (22%) and SCC (40%) were significantly more likely to be COX-2 immunopositive ($P < 0.01$). The fraction of proliferating endothelial cells and the Chalkley scores paralleled multistage carcinogenesis ($P < 0.05$ between different stages). COX-2 immunopositivity was fairly correlated with hypoxia and higher proliferating endothelial cell fractions but not with Chalkley counts. CONCLUSIONS: Induction of COX-2 expression and angiogenesis are both early events in the development of SCC. In addition to ultraviolet light, hypoxia and COX-2 may be involved in skin tumour angiogenesis.

L21 ANSWER 11 OF 24 MEDLINE on STN

AB BACKGROUND: Angiogenesis is a prerequisite for growth of invasive tumours. We hypothesized that angiogenesis would be present in invasive basal cell carcinoma (BCC) but not in a noninvasive tumour such as actinic keratosis (AK). OBJECTIVES: To investigate both types of tumour for evidence of angiogenesis. METHODS: Patients with BCC or AK underwent intravital videocapillaroscopy. Three regions were examined: the tumour, perilesional skin and a control site. Microvessel width, area fraction and length density were determined from capillaroscopy images. Biopsies were stained for CD34 and a microvessel count was performed. RESULTS: Capillaroscopy demonstrated a grossly disorganized tumour microcirculation in BCC. Compared with control skin, microvessel width was increased 2.4-fold, area fraction was increased 4.9-fold and length density was increased 5.9-fold. In AK, microvessel width was increased 1.7-fold, area fraction 2.5-fold and length density 3.4-fold. Vessel width and area fraction were significantly greater in BCC than AK. Biopsies showed significant increases in microvessel length density for both BCC and AK compared with control skin, with BCC significantly greater than AK. CONCLUSIONS: Angiogenesis was demonstrated in BCC in humans in vivo, and to a lesser extent in AK.

L21 ANSWER 12 OF 24 MEDLINE on STN

AB Sturge-Weber syndrome (SWS) is a neurocutaneous disorder that presents with a facial port-wine stain and a leptomeningeal angioma. Fibronectin expression regulates angiogenesis and vasculogenesis and participates in brain tissue responses to ischemia and seizures. We therefore hypothesized that abnormal gene expression of fibronectin and other extracellular matrix genes would be found in SWS brain tissue and SWS port-wine skin fibroblasts. Fibronectin gene and protein expression from port-wine-derived fibroblasts were compared with that from normal skin-derived fibroblasts of four individuals with SWS using microarrays, reverse transcriptase-PCR, Western analysis, and immunocytochemistry. Fibronectin gene and/or protein expression from eight SWS surgical brain samples was compared with that in two surgical epilepsy brain samples and six postmortem brain samples using microarrays, reverse transcriptase-PCR, and Western analysis. The gene expression of fibronectin was significantly increased ($p < 0.05$) in the SWS port-wine-derived fibroblasts compared with that of fibroblasts from SWS normal skin. A trend for increased protein levels of fibronectin in port-wine fibroblasts was found by Western analysis. No difference in the pattern of fibronectin staining was detected. The gene expression of

fibronectin was significantly increased ($p < 0.05$), and a trend for increased fibronectin protein expression was found in the SWS surgical brain samples compared with the postmortem controls. These results suggest a potential role for fibronectin in the pathogenesis of SWS and in the brain's response to chronic ischemic injury in SWS. The reproducible differences in fibronectin gene expression between the SWS port-wine-derived fibroblasts and the SWS normal skin-derived fibroblasts are consistent with the presence of a hypothesized somatic mutation underlying SWS.

L21 ANSWER 13 OF 24 MEDLINE on STN

AB Renal angiomyolipomas are common in patients with tuberous sclerosis complex (TSC), and the risk of severe haemorrhage from these angiomyolipomas can become substantial. This case illustrates a potentially life-threatening condition due to the development of a large aneurysm within an angiomyolipoma, which was discovered within 14 months of her screening renal ultrasound scan. Renal arterial embolisation and renal sparing surgery resulted in good recovery. Clear guidelines for the screening, surveillance, and treatment of angiomyolipomas in patients with TSC are required. This includes the appropriate frequency of surveillance for patients in different age groups and at different stages of angiomyolipoma development, based on a growing knowledge of the natural history of this condition, since growth of renal angiomyolipomas can be rapid and asymptomatic. Computed tomography or magnetic resonance imaging may be required to demonstrate complications in large lesions, as three ultrasound examinations in this patient failed to detect the large aneurysm which had developed. Angiogenesis inhibitors could potentially play a role in preventing the development of angiomyolipomas, which could improve the prognosis for patients with TSC and therefore warrants investigation through phase II/III clinical trials.

L21 ANSWER 14 OF 24 MEDLINE on STN

AB Protein kinase B (PKB) has emerged as the focal point for many signal transduction pathways, regulating multiple cellular processes such as glucose metabolism, transcription, apoptosis, cell proliferation, angiogenesis, and cell motility. In addition to acting as a kinase toward many substrates involved in these processes, PKB forms complexes with other proteins that are not substrates, but rather act as modulators of PKB activity and function. In this review, we discuss the implications of these data in understanding the multitude of functions predicted for PKB in cells.

L21 ANSWER 15 OF 24 MEDLINE on STN

AB BACKGROUND: Tuberous sclerosis is an autosomal dominant condition characterized by the development of benign neoplasms of the brain, kidney, and skin. Progressive growth and malignant transformation of brain and kidney lesions constitute the major cause of morbidity and mortality in adults with tuberous sclerosis. In addition, growth of skin lesions may be disfiguring to patients. OBJECTIVE: The purpose of this study was to determine whether benign tumors in patients with tuberous sclerosis are angiogenic. METHODS: Brain, kidney, and skin tumors from patients with tuberous sclerosis were stained with CD31, a specific marker of vascular endothelium. In addition, we used Northern blot analysis to demonstrate that renal angiomyolipoma cells express the potent angiogenesis stimulator vascular endothelial growth factor (VEGF). RESULTS: Brain, kidney, and skin neoplasms from patients with tuberous sclerosis are highly angiogenic. Renal angiomyolipoma cells produce the potent angiogenic factor VEGF. CONCLUSION: Benign neoplasms of patients with tuberous sclerosis are highly vascular. Our results provide a rationale for antiangiogenic therapy in the treatment and prevention of tuberous sclerosis-associated neoplasms.

L21 ANSWER 16 OF 24 MEDLINE on STN

AB BACKGROUND: Tuberous sclerosis complex (TSC) is an autosomal dominantly inherited disorder associated with an alteration of the TSC2 tumor suppressor gene which encodes for the protein product tuberin. The disease is characterized by the development of hamartomas, e.g. cutaneous angiofibromas which consist of vascular cells, interstitial cells, and normal components of the skin. The Eker rat model, an animal model of inherited cancer, has been shown to carry a mutation of TSC2. METHODS: Immunohistochemical analyses of human angiofibromas were performed using antibodies directed against tuberin and angiogenic growth factors. Proliferation of human dermal microvascular endothelial cells (HDMEC) was determined after incubation with the supernatants of TSC2 (+/+) and TSC2 (-/-) rat embryonic fibroblasts (REF) that were derived from the Eker strain. RESULTS: Loss of the expression of tuberin was observed in the interstitial cells of 13 of 39 angiofibromas. The expression of tuberin was retained in the vascular cells. In all analyzed angiofibromas, the angiogenic factors bFGF, PD-ECGF, VEGF and angiogenin were detected in the interstitial cells and/or vascular cells. Expression of PDGF-B and TGF-beta1 was weak. Tissue culture supernatants from TSC2 (-/-) REF stimulated the growth of HDMEC significantly more than supernatants from TSC2 (+/+) REF. CONCLUSION: A functional loss of tuberin may stimulate vascular growth.

L21 ANSWER 17 OF 24 MEDLINE on STN

AB Angiogenesis is a crucial event in carcinogenesis and its onset has been associated with premalignant tumour stages. In order to elucidate the significance of angiogenesis in different stages of epithelial skin tumours, we analysed the vessel density in ten normal skin samples, 14 actinic keratosis (AK), 12 hypertrophic AKs, and in nine early- and 16 late-stage squamous cell carcinomas (SCCs). Mean vascular density was quantitated by counting the number of CD 31-immunostained blood vessels and by morphometric assessment of stained vessel area by computer-assisted image analysis. The results from both methods were well correlated. Mean vascular density was similar in normal dermis and in AK, and only slightly elevated in hypertrophic AKs and early SCC stages (tumour thickness < 2 mm). Only late-stage SCCs infiltrating the subcutis exhibited a significant increase in vascularization. Vessel density was independent of tumour localization, degree of proliferation and inflammatory cell infiltration. Furthermore, tumour vascularization was not correlated with the expression of vascular endothelial growth factor, a major angiogenic factor, as revealed by in situ hybridization and immunohistochemistry. The restriction of enhanced vascularization to increased tumour thickness may be a major reason for the rather low metastatic spread of cutaneous SCCs.

L21 ANSWER 18 OF 24 MEDLINE on STN

AB Hemangiomas and vascular malformations are frequently encountered in pediatric practice, especially hemangiomas and port-wine stains. These lesions may cause physical and psychological complications and it is important to recognize which lesions need to be treated and how. Great progress has been made in the classification of vascular anomalies. Angiogenesis and molecular genetics are areas of active research; recent findings relating to hemangiomas and vascular malformations are presented. New clinical features of hemangiomas are described, such as association of extensive facial hemangiomas with various malformations and the occurrence of Kasabach-Merritt phenomenon, not with common hemangiomas, but with other vascular tumors (Kaposiform hemangioendothelioma and tufted angioma). Interferon alfa is effective for treatment of complicated hemangiomas but may cause serious neurological side effects. It is to be hoped that early diagnosis of Sturge-Weber syndrome will soon be possible with new, noninvasive, functional imaging techniques. New issues surrounding pulsed dye laser therapy for port-wine stains are also discussed in this article.

L21 ANSWER 19 OF 24 MEDLINE on STN

AB The protooncogene c-myc regulates cell growth, differentiation, and apoptosis, and its aberrant expression is frequently observed in human cancer. However, the consequences of activating c-Myc in an adult tissue, in which these cellular processes are part of normal homeostasis, remain unknown. In order to achieve this, we have targeted expression of a switchable form of the c-Myc protein to the skin epidermis, a well characterized homeostatic tissue. We show that activation of c-MycER in adult suprabasal epidermis rapidly triggers proliferation and disrupts differentiation of postmitotic keratinocytes. Sustained activation of c-Myc is sufficient to induce papillomatosis together with angiogenesis--changes that resemble hyperplastic actinic keratosis, a commonly observed human precancerous epithelial lesion. All these premalignant changes spontaneously regress upon deactivation of c-MycER.

L21 ANSWER 20 OF 24 MEDLINE on STN

AB Topical gel containing 3% diclofenac in 2.5% hyaluronic acid (HYAL CT1101) is used for the treatment of actinic keratosis. In animal models, diclofenac in hyaluronic acid inhibited angiogenesis and induced neovascular regression in inflammatory tissue, and depleted substance P content in snout tissue. Diclofenac delivered in hyaluronic acid appears to accumulate in the epidermis of human skin in vitro and mice in vivo. Results of clinical trials indicate that topical HYAL CT1101 is effective in the treatment of actinic keratosis. A clinical cure (all lesions fully resolved) was seen in 47% of 108 patients using HYAL CT1101 compared with 19% of patients using placebo after 3 months in 1 randomised, double-blind study. Mild to moderate skin irritation has been reported in up to 72% of patients treated with HYAL CT1101 in clinical studies.

L21 ANSWER 21 OF 24 MEDLINE on STN

AB A case of phacomatosis pigmentovascularis (PPV) in a 6-year-old girl with Sturge-Weber syndrome, pyogenic granuloma, and other complications is described. It is relatively rare that a complete form of Sturge-Weber syndrome was associated with PPV. A review of the literature on PPV, focusing on total number of reported cases and etiological speculations, is presented. To our knowledge, a total of 118 cases of PPV, including the present one, have been reported to date. Regardless of many speculations, the true etiology remains unknown. The average "density" of mast cells (MCs) per mm2 appearing in the central region of the pyogenic granuloma was calculated to be 86.3/mm2 and that in the adjacent nevus flammeus was 37.9/mm2. The "density" of mast cells in pyogenic granuloma separately calculated from ten other cases was 105.5 +/- 28.6/mm2 (mean +/- SD), compared with that in normal skin, 6.85 +/- 4.9/mm2 (n = 20). There was a significant difference between the two, indicating that MCs are closely associated with angiogenesis in pyogenic granuloma.

L21 ANSWER 22 OF 24 MEDLINE on STN

AB Topical diclofenac in 2.5% hyaluronan inhibits basal cell carcinoma, actinic keratosis, and murine colon-26 growth in vivo. colon-26 tumor growth was preceded by angiogenesis and reduced apoptotic and mitotic indices. Diclofenac reduced proliferation and viability in vitro, and stimulated apoptosis. Hyaluronan inhibited proliferation and viability at 1 mg/ml but was inactive below this level. Topical application of diclofenac inhibited tumor prostaglandin synthesis and retarded angiogenesis and tumor growth (ratio of treatment:control, 0.174). The mitotic index remained unaltered in vivo, whereas the apoptotic index and necrosis were increased. Topical vehicle exhibited slight antitumor and antiangiogenesis activity. The substantial quantities of diclofenac delivered locally in hyaluronan may exhibit antitumor activity in similar fashion to those seen in vitro and explain its clinical efficacy.

L21 ANSWER 23 OF 24 MEDLINE on STN
AB In a novel application, hyaluronan has been utilized as a delivery system for topical and i.v. therapeutics. Clinical trials and case reports show that topical diclofenac delivered in hyaluronan (HYAL CT-1101) is effective against basal-cell carcinoma and actinic keratosis. The effect of this drug formulation on tumour growth and angiogenesis, as well as granulomatous tissue angiogenesis, has been investigated experimentally. The evidence that hyaluronan has a permissive effect on the inhibition of granulomatous tissue angiogenesis by diclofenac (as assessed by the carminel/gelatin vascular casting method) when injected into the lesion or applied topically is reviewed. Topical diclofenac in hyaluronan also induces a regression of the existing neo-vasculature of granulomatous tissue when applied therapeutically. The diclofenac formulated in hyaluronan was also found to be profoundly effective against the development of subcutaneous Colon-26 tumours in syngeneic balb/c mice (T/C ratio after 12 days topical application of 0.174, $p < 0.0001$). Analysis of the tumour vasculature showed that vascular development was retarded by 12 days. This was shown by the reduction in the tumour density of carmine in the vascular casts, as well as reduced blood-vessel density visualized by rat anti-mouse CD31 immunohistology. Hyaluronan alone had a significant effect on tumour development with a 50% inhibition of tumour growth and only a transient reduction in vascularity. The effects noted when diclofenac is formulated in hyaluronan, and applied topically, could be related to trans-dermal delivery and deposition properties of hyaluronan, and to the binding properties of hyaluronan to areas of pathology with high expression of hyaluronan receptors such as RHAMM, ICAM-1, and CD44.

L21 ANSWER 24 OF 24 MEDLINE on STN
AB We examined alpha-actin and an angiogenic factor, basic fibroblast growth factor (bFGF), by immunohistochemistry and Western blot analysis in four angiofibromas (AFs) and a connective tissue nevus (CTN) obtained from two patients with tuberous sclerosis (TS). There was an increase of alpha-actin-positive microvessels in the papillary and the upper reticular dermis of AFs and a CTN as compared to those in normal skin. The main localization of alpha-actin in the microvessels of AFs was considered to be pericytes. Many microvessels and a few interstitial fibroblast-like cells in frozen sections of AFs and a CTN were positively stained for bFGF, and most of the bFGF-positive microvessels corresponded to those containing alpha-actin as determined by double immunostaining. These data suggested a possible role of increased bFGF in stimulating angiogenesis and/or mainitaining vessels in AFs, although augmentation of mitotic activity was not noted by staining with Ki-67. Further investigations on the identification of the bFGF-producing cells and biological function of bFGF in AFs may be a clue to elucidate pathomechanisms of AFs.

=> d 1-24

L21 ANSWER 1 OF 24 MEDLINE on STN
AN 2007020754 MEDLINE
DN PubMed ID: 17204940
TI Upregulation of hypoxia-inducible factor (HIF)-1alpha and HIF-2alpha in leptomeningeal vascular malformations of Sturge-Weber syndrome.
AU Comati Amina; Beck Heike; Halliday William; Snipes G Jackson; Plate Karl Heinz; Acker Till
CS Edinger Institute, Frankfurt, Germany.
SO Journal of neuropathology and experimental neurology, (2007 Jan) Vol. 66, No. 1, pp. 86-97.
Journal code: 2985192R. ISSN: 0022-3069.

CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200702
ED Entered STN: 13 Jan 2007
Last Updated on STN: 16 Feb 2007
Entered Medline: 15 Feb 2007

L21 ANSWER 2 OF 24 MEDLINE on STN
AN 2007008607 MEDLINE
DN PubMed ID: 17110594
TI Hypoxia-induced endothelial proliferation requires both mTORC1 and mTORC2.
AU Li Weimin; Petrimpol Marco; Molle Klaus D; Hall Michael N; Battegay Edouard J; Humar Rok
CS Department of Research, University Hospital Basel, Hebelstrasse 20, CH-4031 Basel, Switzerland.
SO Circulation research, (2007 Jan 5) Vol. 100, No. 1, pp. 79-87. Electronic Publication: 2006-11-16.
Journal code: 0047103. E-ISSN: 1524-4571.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200702
ED Entered STN: 6 Jan 2007
Last Updated on STN: 2 Feb 2007
Entered Medline: 1 Feb 2007

L21 ANSWER 3 OF 24 MEDLINE on STN
AN 2006607697 MEDLINE
DN PubMed ID: 16824050
TI Inflammation of actinic keratoses subsequent to therapy with sorafenib, a multitargeted tyrosine-kinase inhibitor.
AU Lacouture M E; Desai A; Soltani K; Petronic-Rosic V; Laumann A E; Ratain M J; Stadler W M
CS Section of Dermatology, Department of Medicine, University of Chicago, IL, USA.. m-lacouture@northwestern.edu
SO Clinical and experimental dermatology, (2006 Nov) Vol. 31, No. 6, pp. 783-5. Electronic Publication: 2006-07-04.
Journal code: 7606847. ISSN: 0307-6938.
CY England: United Kingdom
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200703
ED Entered STN: 17 Oct 2006
Last Updated on STN: 30 Mar 2007
Entered Medline: 29 Mar 2007

L21 ANSWER 4 OF 24 MEDLINE on STN
AN 2006575802 MEDLINE
DN PubMed ID: 16958055
TI Vascular update: morphogenesis, tumors, malformations, and molecular dimensions.
AU Cohen M Michael Jr
CS Department of Pediatrics, Dalhousie University, 5981 University Ave., Halifax, Nova Scotia B3H 1W2.. michael.cohen@dal.ca
SO American journal of medical genetics. Part A, (2006 Oct 1) Vol. 140, No. 19, pp. 2013-38. Ref: 152

Journal code: 101235741. ISSN: 1552-4825.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200611
ED Entered STN: 29 Sep 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 29 Nov 2006

L21 ANSWER 5 OF 24 MEDLINE on STN
AN 2006134850 MEDLINE
DN PubMed ID: 16470587
TI Genetic alterations in urothelial bladder carcinoma: an updated review.
AU Mhawech-Fauceglia Paulette; Cheney Richard T; Schwaller Juerg
CS Department of Pathology and Laboratory Medicine, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA.. pmhawech1@yahoo.com
SO Cancer, (2006 Mar 15) Vol. 106, No. 6, pp. 1205-16. Ref: 101
Journal code: 0374236. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200605
ED Entered STN: 9 Mar 2006
Last Updated on STN: 5 May 2006
Entered Medline: 4 May 2006

L21 ANSWER 6 OF 24 MEDLINE on STN
AN 2005621287 MEDLINE
DN PubMed ID: 16302556
TI Imiquimod as an antiangiogenic agent.
AU Li Vincent W; Li William W; Talcott Katherine E; Zhai Amy W
CS The Angiogenesis Foundation, Cambridge, MA 02238, USA.. vli@angio.org
SO Journal of drugs in dermatology : JDD, (2005 Nov-Dec) Vol. 4, No. 6, pp. 708-17. Ref: 53
Journal code: 101160020. ISSN: 1545-9616.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200601
ED Entered STN: 24 Nov 2005
Last Updated on STN: 11 Jan 2006
Entered Medline: 10 Jan 2006

L21 ANSWER 7 OF 24 MEDLINE on STN
AN 2005489438 MEDLINE
DN PubMed ID: 16159522
TI Sturge-Weber syndrome: altered blood vessel fibronectin expression and morphology.
AU Comi Anne M; Weisz Catherine J C; Highet Bridget H; Skolasky Richard L; Pardo Carlos A; Hess Ellen J
CS Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA.. acomi@jhmi.edu
NC K12NS01696 (NINDS)
SO Journal of child neurology, (2005 Jul) Vol. 20, No. 7, pp. 572-7.
Journal code: 8606714. ISSN: 0883-0738.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200510
ED Entered STN: 15 Sep 2005
Last Updated on STN: 21 Oct 2005
Entered Medline: 20 Oct 2005

L21 ANSWER 8 OF 24 MEDLINE on STN
AN 2005478428 MEDLINE
DN PubMed ID: 16129702
TI MCP-1 overexpressed in tuberous sclerosis lesions acts as a paracrine factor for tumor development.
AU Li Shaowei; Takeuchi Fumiko; Wang Ji-an; Fuller Christopher; Pacheco-Rodriguez Gustavo; Moss Joel; Darling Thomas N
CS Department of Dermatology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA.
NC 1 R01 CA100907 (NCI)
R01 CA100907-01A1 (NCI)
SO The Journal of experimental medicine, (2005 Sep 5) Vol. 202, No. 5, pp. 617-24. Electronic Publication: 2005-08-29.
Journal code: 2985109R. ISSN: 0022-1007.
CY United States
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200602
ED Entered STN: 9 Sep 2005
Last Updated on STN: 28 Feb 2006
Entered Medline: 27 Feb 2006

L21 ANSWER 9 OF 24 MEDLINE on STN
AN 2005179519 MEDLINE
DN PubMed ID: 15811118
TI Peroxisome proliferator-activated receptors in squamous cell carcinoma and its precursors.
AU Nijsten Tamar; Geluyckens Elke; Colpaert Cecile; Lambert Julien
CS Department of Dermatology, University Hospital Antwerp, Antwerp, Belgium.. tamar.nijsten@uza.be
SO Journal of cutaneous pathology, (2005 May) Vol. 32, No. 5, pp. 340-7.
Journal code: 0425124. ISSN: 0303-6987.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200508
ED Entered STN: 7 Apr 2005
Last Updated on STN: 9 Aug 2005
Entered Medline: 8 Aug 2005

L21 ANSWER 10 OF 24 MEDLINE on STN
AN 2004520799 MEDLINE
DN PubMed ID: 15491425
TI Cyclooxygenase-2 expression and angiogenesis in squamous cell carcinoma of the skin and its precursors: a paired immunohistochemical study of 35 cases.
AU Nijsten T; Colpaert C G; Vermeulen P B; Harris A L; Van Marck E; Lambert J
CS Pathology, University of Antwerp, Antwerp, Belgium.
SO The British journal of dermatology, (2004 Oct) Vol. 151, No. 4, pp.

837-45.
Journal code: 0004041. ISSN: 0007-0963.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200502
ED Entered STN: 20 Oct 2004
Last Updated on STN: 8 Feb 2005
Entered Medline: 7 Feb 2005

L21 ANSWER 11 OF 24 MEDLINE on STN
AN 2003384414 MEDLINE
DN PubMed ID: 12890202
TI Comparison of the microvasculature of basal cell carcinoma and actinic keratosis using intravital microscopy and immunohistochemistry.
AU Newell B; Bedlow A J; Cliff S; Drysdale S B; Stanton A W B; Mortimer P S
CS Division of Physiological Medicine (Dermatology), St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, U.K.
SO The British journal of dermatology, (2003 Jul) Vol. 149, No. 1, pp. 105-10.
Journal code: 0004041. ISSN: 0007-0963.
CY England: United Kingdom
DT (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 19 Aug 2003
Last Updated on STN: 10 Oct 2003
Entered Medline: 9 Oct 2003

L21 ANSWER 12 OF 24 MEDLINE on STN
AN 2003193372 MEDLINE
DN PubMed ID: 12621118
TI Increased fibronectin expression in sturge-weber syndrome fibroblasts and brain tissue.
AU Comi Anne M; Hunt Piper; Vawter Marquis P; Pardo Carlos A; Becker Kevin G; Pevsner Jonathan
CS Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA.. acomi@jhmi.edu
NC HD24061 (NICHD)
K12NS01696 (NINDS)
SO Pediatric research, (2003 May) Vol. 53, No. 5, pp. 762-9. Electronic Publication: 2003-03-05.
Journal code: 0100714. ISSN: 0031-3998.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200312
ED Entered STN: 26 Apr 2003
Last Updated on STN: 17 Dec 2003
Entered Medline: 4 Dec 2003

L21 ANSWER 13 OF 24 MEDLINE on STN
AN 2002707135 MEDLINE
DN PubMed ID: 12469175
TI Management of renal angiomyolipoma in patients with tuberous

sclerosis complex.
AU Simmons J L; Hussain S A; Riley P; Wallace D M A
CS University Hospital Birmingham, Edgbaston, UK.
SO Oncology reports, (2003 Jan-Feb) Vol. 10, No. 1, pp. 237-41.
Journal code: 9422756. ISSN: 1021-335X.
CY Greece
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 17 Dec 2002
Last Updated on STN: 8 Jun 2003
Entered Medline: 6 Jun 2003

L21 ANSWER 14 OF 24 MEDLINE on STN
AN 2002659584 MEDLINE
DN PubMed ID: 12419241
TI PKB binding proteins. Getting in on the Akt.
AU Brazil Derek P; Park Jongsun; Hemmings Brian A
CS Friedrich Miescher Institute for Biomedical Research, Maulbeerstrasse 66, CH-4058 Basel, Switzerland.
SO Cell, (2002 Nov 1) Vol. 111, No. 3, pp. 293-303. Ref: 87
Journal code: 0413066. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 7 Nov 2002
Last Updated on STN: 19 Dec 2002
Entered Medline: 18 Dec 2002

L21 ANSWER 15 OF 24 MEDLINE on STN
AN 2002158115 MEDLINE
DN PubMed ID: 11862172
TI Tuberous sclerosis-associated lesions of the kidney, brain, and skin are angiogenic neoplasms.
AU Arbiser Jack L; Brat Daniel; Hunter Steve; D'Armiento Jeanine; Henske Elizabeth P; Arbiser Zoya K; Bai Xianhe; Goldberg Gerald; Cohen Cynthia; Weiss Sharon W
CS Department of Dermatology, Emory University School of Medicine, WMB 5309, 1639 Pierce Street, Atlanta, GA 30322, USA.. jarbise@emory.edu
NC AR 02030 (NIAMS)
AR 47901 (NIAMS)
P30 AR 42687 (NIAMS)
SO Journal of the American Academy of Dermatology, (2002 Mar) Vol. 46, No. 3, pp. 376-80.
Journal code: 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 14 Mar 2002
Last Updated on STN: 3 Apr 2002
Entered Medline: 27 Mar 2002

L21 ANSWER 16 OF 24 MEDLINE on STN
AN 2001565594 MEDLINE

DN PubMed ID: 11553313
TI Loss of tuberin, the tuberous-sclerosis-complex-2 gene product is associated with angiogenesis.
AU Nguyen-Vu P A; Fackler I; Rust A; DeClue J E; Sander C A; Volkenandt M; Flaig M; Yeung R S; Wienecke R
CS Department of Dermatology, Ludwig-Maximilians-University Munich, Munich, Germany.
SO Journal of cutaneous pathology, (2001 Oct) Vol. 28, No. 9, pp. 470-5. Journal code: 0425124. ISSN: 0303-6987.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 24 Oct 2001
Last Updated on STN: 24 Jan 2002
Entered Medline: 31 Dec 2001

L21 ANSWER 17 OF 24 MEDLINE on STN
AN 2000144876 MEDLINE
DN PubMed ID: 10682671
TI Angiogenic switch occurs late in squamous cell carcinomas of human skin.
AU Strieth S; Hartschuh W; Pilz L; Fusenig N E
CS Division of Differentiation and Carcinogenesis, German Cancer Research Center (DKFZ), Heidelberg.
SO British journal of cancer, (2000 Feb) Vol. 82, No. 3, pp. 591-600. Journal code: 0370635. ISSN: 0007-0920.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 14 Mar 2000
Last Updated on STN: 14 Mar 2000
Entered Medline: 2 Mar 2000

L21 ANSWER 18 OF 24 MEDLINE on STN
AN 2000022525 MEDLINE
DN PubMed ID: 10555599
TI Update on hemangiomas and vascular malformations.
AU Powell J
CS University of Montreal, Sainte-Justine Hospital, Pediatric Dermatology Service, Quebec, Canada.
SO Current opinion in pediatrics, (1999 Oct) Vol. 11, No. 5, pp. 457-63. Ref: 41
Journal code: 9000850. ISSN: 1040-8703.
CY United States
DT Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 13 Jan 2000
Last Updated on STN: 13 Jan 2000
Entered Medline: 3 Dec 1999

L21 ANSWER 19 OF 24 MEDLINE on STN
AN 1999288445 MEDLINE
DN PubMed ID: 10360173
TI Reversible activation of c-Myc in skin: induction of a complex neoplastic phenotype by a single oncogenic lesion.
AU Pelengaris S; Littlewood T; Khan M; Elia G; Evan G

CS Imperial Cancer Research Fund, London, United Kingdom..
s.pelengaris@icrf.icnet.uk
SO Molecular cell, (1999 May) Vol. 3, No. 5, pp. 565-77.
Journal code: 9802571. ISSN: 1097-2765.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 28 Jun 1999
Last Updated on STN: 28 Jun 1999
Entered Medline: 17 Jun 1999

L21 ANSWER 20 OF 24 MEDLINE on STN
AN 1999252802 MEDLINE
DN PubMed ID: 10319244
TI Diclofenac/hyaluronic acid.
AU Peters D C; Foster R H
CS Adis International Limited, Auckland, New Zealand.. demail@adis.co.nz
SO Drugs & aging, (1999 Apr) Vol. 14, No. 4, pp. 313-9; discussion 320-1.
Ref: 26
Journal code: 9102074. ISSN: 1170-229X.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 27 Jul 1999
Last Updated on STN: 27 Jul 1999
Entered Medline: 15 Jul 1999

L21 ANSWER 21 OF 24 MEDLINE on STN
AN 1999080653 MEDLINE
DN PubMed ID: 9863285
TI Phacomatosis pigmentovascularis type IIb associated with Sturge-Weber syndrome and pyogenic granuloma.
AU Hagiwara K; Uezato H; Nonaka S
CS Department of Dermatology, Faculty of Medicine, University of the Ryukyus, Okinawa, Japan.
SO The Journal of dermatology, (1998 Nov) Vol. 25, No. 11, pp. 721-9. Ref: 26
Journal code: 7600545. ISSN: 0385-2407.
CY Japan
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 2 Feb 1999
Last Updated on STN: 2 Feb 1999
Entered Medline: 21 Jan 1999

L21 ANSWER 22 OF 24 MEDLINE on STN
AN 97280669 MEDLINE
DN PubMed ID: 9134996
TI The inhibition of colon-26 adenocarcinoma development and angiogenesis by topical diclofenac in 2.5% hyaluronan.
AU Seed M P; Brown J R; Freemantle C N; Papworth J L; Colville-Nash P R; Willis D; Somerville K W; Asculai S; Willoughby D A
CS Department of Experimental Pathology, Saint Bartholomew's Hospital and the Royal London School of Medicine and Dentistry, United Kingdom..

m.p.seed@mds.qmw.ac.uk
SO Cancer research, (1997 May 1) Vol. 57, No. 9, pp. 1625-9.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 2 Jun 1997
Last Updated on STN: 2 Jun 1997
Entered Medline: 21 May 1997

L21 ANSWER 23 OF 24 MEDLINE on STN
AN 97021286 MEDLINE
DN PubMed ID: 8867646
TI The modulation of granulomatous tissue and tumour angiogenesis by diclofenac in combination with hyaluronan (HYAL EX-0001).
AU Freemantle C; Alam C A; Brown J R; Seed M P; Willoughby D A
CS Department of Experimental Pathology, Saint Bartholomew's Hospital Medical College, London, United Kingdom.
SO International journal of tissue reactions, (1995) Vol. 17, No. 4, pp. 157-66. Ref: 51
Journal code: 8302116. ISSN: 0250-0868.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199701
ED Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 3 Jan 1997

L21 ANSWER 24 OF 24 MEDLINE on STN
AN 92015836 MEDLINE
DN PubMed ID: 1656117
TI Increase in alpha-actin and basic fibroblast growth factor in angiofibromas in patients with tuberous sclerosis.
AU Takanashi M; Nakayama J; Inoue M; Urabe A; Hori Y
CS Department of Dermatology, School of Medicine, Kyushu University.
SO Nippon Hifuka Gakkai zasshi. The Japanese journal of dermatology, (1991 May) Vol. 101, No. 6, pp. 601-8.
Journal code: 7600571. ISSN: 0021-499X.
CY Japan
DT (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA Japanese
FS Priority Journals
EM 199110
ED Entered STN: 24 Jan 1992
Last Updated on STN: 3 Feb 1997
Entered Medline: 28 Oct 1991